BRAIN.

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Original Articles and Clinical Cases.

REMARKS ON THE REFLEX MECHANISM OF THE STEP.[1]

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To an observer who would analyse them, the acts of walking, running, and of progression in its various forms present themselves in every case as actions compounded of a posture and a movement. In such acts we see particularly clearly exemplified a twofold activity of the nervous system. An activity which uses the musculature to maintain static effects — postures, and an activity which uses it to produce kinetic effects—movements. Thus, the static component in walking is maintenance of the erect posture; the kinetic component is a rhythmic alternating movement of the limbs—stepping. This static component is closely related to that which constitutes standing, so closely, in fact, that such acts as walking and running may for analysis be conveniently regarded as the postural act of standing upon which there are grafted rhythmic flexion-extension movements of each limb in turn, resulting in locomotion.

In their importance to the existence of the individual and the species the acts of standing and progression seem among all the work of the striped muscles, to rank second only to that of respiratory ventilation of the lung, and the actual prehension of food by the mouth. Their prime importance and their inherent, though in man post-natal, development suggest that in essence the organization of these acts must, even in man, be purely reflex. The belief is, indeed, general that such an act as walking, when stripped of extraneous regulative

[1] Presidential Address to the Neurological Section of the Royal Society of Medicine.

influences which can start, restrain, modify, and adjust it to varied circumstances, has at basis a fundamental mechanism of purely reflex operation.

That the act of walking is not dependent on the integrity of the cerebral cortex has long been proved experimentally by well-known experiments on the lower vertebrates, and on mammals even of such high type as the dog. In the dog Goltz removed both cerebral hemispheres to such an extent that only the basal part of the two temporal lobes remained, and these remnants, with the corpora striata and parts of the optic thalami and anterior colliculi, were in a condition of detritus and softening when the autopsy was made. This dog was yet able to walk, and did, indeed, walk "spontaneously."

It seems clear that inquiry regarding the mechanism executive of such an act as reflex walking must include search for a postural reflex which will also underlie the act of standing, and for a purely reflex limb-movement which will be the essential reflex of the step.

As to the former of these, the postural reflex, experimental search meets with a positive result as follows. When all of the brain in front of a transection between anterior and posterior colliculi is removed in a cat or dog, the decerebrate preparation thus obtained exhibits a systemic postural reflex with the following features. The extensor muscles of all four limbs, the dorsal muscles of the back, neck, and tail, the retractors of the head, and the elevators of the lower jaw, are all in harmoniously co-ordinated steady tonic contraction. This contraction is reflex, for it is at once abolished in each local region by severance of the afferent spinal roots of that region; for instance, in a limb by severance of the afferent spinal roots of that limb, in the neck by severance of the afferent roots of the neck, and so on. So local is its reflex-origin that in the extensor muscle of the knee, for instance, it is *essentially* dependent on the afferent nerve of that muscle, and on no other afferent nerve. It can be increased through other afferent channels, but is not essentially dependent on them. In this tonic reflex, though all the above-mentioned groups of muscles—they may briefly be termed extensors—exhibit the tonic contraction, their antagonists do not exhibit contraction. On the contrary, they appear to lie under a tonic reflex inhibition, which keeps them in a state of slight relaxation, the converse of the mild, persistent contraction of the extensors. This widespread tonic reflex which constitutes decerebrate rigidity does not draw its source from skin-afferents; its origin is traceable to the deep afferents, especially those belonging to the extensor muscles themselves,

exhibiting the reflex tonus. The postural reflex is, in fact, a proprioceptive reflex.

The muscles exhibiting the steady contraction executing this general reflex, although they are widely distributed in the body, compose nevertheless a homogeneous system. They all by their contraction contribute to one common result. They each and all, by contracting, counteract gravity in the ordinary erect position usual to the animal, the *ususstatus*.[1]

In the limbs they keep the limb from yielding under its own weight and under that of the body superimposed. In neck and head they keep those parts from falling; similarly in the tail they keep it from dropping, and in the head they keep the lower jaw in apposition to the upper, so that the mouth is closed. In fact, their reflex tonus is, as I have pointed out elsewhere [7], simply the expression of a maintained posture.[2] If the preparation be passively set upright on its feet the systemic tonic reflex suffices to support it in the erect posture. In short, the postural reflex is "standing" executed purely reflexly. The decerebrate preparation maintains its "standing" attitude even for hours at a time.

The decerebrate preparation possesses the otic labyrinths and nervi octavi. It might be thought that these great receptors and their afferent apparatus were responsible for the standing reflex which the preparation exhibits. The beautiful researches of Ewald have shown the widely distributed tonic influences which these organs can exert. But the decerebrate preparation still continues to stand when the otic labyrinths have been destroyed or the octavi cut. This is so both when the labyrinths are removed or octavi severed subsequent to decerebration and appearance of the static postural reflex, and also when the labyrinths have been destroyed or octavi cut a short time prior to the decerebration. In the latter case my observations, in several of which I have to thank Dr. S. Sewell for invaluable co-operation, have at present dealt with decerebration practised at a short interval only after ablation of the labyrinths. The longest periods were in one case decerebration four days after removal of both labyrinths, and in another eight days after removal of left labyrinth and two days after removal of the right. These lesions did not prevent the full postural reflex from ensuing on decerebration, nor did they even impair it noticeably. Reflex standing still engaged the preparation. These results, so far as they go, agree with the further fact that the decerebrate preparation still continues to exhibit the postural reflex of "standing" when laid on its side or even when inverted. In this latter

[1] This convenient term was first introduced by Karl Schaffer [6].
[2] *Cf.* also Lewandowsky [5].

position, however, the reflex posture is not usually, in my experience, maintained for long. That the otic labyrinths can *influence* the postural reflex of the decerebrate preparation is undeniable, but, so far as my observations at present go, they are not responsible for the fundamental execution of the reflex. The reflex can occur without them.

A feature of the reflex tonus which thus executes the posture of standing in the decerebrate preparation is "plasticity." The length of this or that muscle or muscle-group is capable of modification without detriment to or disturbance of the tonic tension of the muscle. Each such local modification is given by an intrinsic proprioceptive reflex. The plasticity appears to meet the requirement that in "standing" the posture of the limb may vary, provided always that each joint maintains a resistance sufficient to counteract the tendency of the superimposed weight it carries to flex it. Ordinary standing postures, especially in the quadruped, include variable degrees of flexion at hip and knee, and the pose of extension is usually greater at the knee. One hind-foot may rest close beside the other or in advance of or behind it. Yet in all cases, though the tonic length of the muscle varies greatly, its tonic tension varies little and does not fall below that required to bear the superincumbent load. In this postural reflex the extensor muscles are, to follow v. Uexküll's terminology, acting as "Sperr-muskeln." Thus in each limb they secure that, in the various positions of the joints in standing, the tension of the muscles shall still continue adjusted to the support the limb requires in the standing animal. Just as the sea-urchin rests supported on its spines by the "Sperrreflex" of the tonic muscles of the spines, so the decerebrate cat and dog stand in virtue of the "Sperrreflex" stiffening the jointed framework of the animal by means of the tonus of the anti-gravity muscles.

This reflex standing disappears when the transection of the brain is made behind the posterior edge of the pons. It is not present, therefore, in the decapitated preparation; the decapitated preparation cannot, so far as I have seen, stand. To decide how far this abolition of the reflex standing is a matter of shock, or how far with lapse of time the ability to stand is recovered, recourse must be had to other preparations than the decapitated. When in the dog the spinal cord is severed in the thoracic region the hind-limbs cannot at first stand; but after lapse of weeks or months they exhibit this power. That is, with hind-feet on the ground the reflex tonus of limb-extension suffices to bear the weight of the limbs and superincumbent hind-quarters. The attitude thus exhibited indubitably amounts to standing and is sometimes maintained for minutes

at a time. But this spinal standing is not fully equivalent to the standing of the decerebrate preparation. It is less steady, is subject to sudden lapses, irregular in intensity, less enduring, and allows less latitude of variation in the exact posture of the limbs. The tonus which executes it is less plastic. Sometimes it cannot be obtained at all. The tonic contraction which executes it is, however, like that of the decerebrate preparation, independent of the cutaneous afferents. It is like that of the decerebrate preparation, a reflex of proprio-ceptive nature.

Experimental search for the postural or static component of walking, considered as a purely reflex act, arrives therefore at a definite result. It finds a tonic postural reflex able to execute the *usustatus* after removal of the whole fore-brain and part of the mid-brain as well. And it finds that a residuum of that reflex *usustatus* is obtainable even as a purely spinal reflex.

Turning now to the other component of walking—the kinetic—responsible for the movements of the step, and looking for a purely reflex reaction as its basis, we may again take as our field the hind-limb, especially since data from it are more immediately applicable to the bipedal progression of man. The hind-limbs of the dog, when the period of shock has passed, after thoracic spinal transection exhibit a rhythmic movement, the similarity of which to stepping was noted by its first investigators, Goltz and Freusberg. Recently the kinematograph analysis of these movements by Philippson has convincingly established their identity with normal stepping.

Similar reflex stepping can also be observed with facility in the decapitated preparation (cat). If the lungs of the carcase of a decapitated cat be appropriately ventilated by bellows, the headless preparation will continue for several hours to exhibit, under appropriate stimuli, various reflexes. A significant feature of such spinal reflexes is that they tend to be of *alternating* form, thus in the limbs their movements exhibit alternating flexion and extension; flexion tends to be followed by extension, this again by flexion, and so on alternately. Among these *alternating reflexes* that of stepping, especially of the hind-limbs, is prominent. An effective stimulus for exciting the stepping movement is pressure by a small spring clip applied to the skin. Certain skin regions provoke the reflex best: for instance, that of perineum or of a foot, but not that of the limb which is to step. The stimulus is continuous and constant, but the reflex response of the musculature engaged in the stepping is rhythmic. Faradization of an afferent nerve will also evoke the reflex stepping. Here the stimulus, though it is essentially rhythmic, has a rate

of rhythm far faster—about 30 per second— than that of the rhythmic movement—about 2 per second—which it evokes. The reflex stepping may be also produced by direct faradization of the cross-section of the lower end of the bulb or top of the spinal cord laid bare by the decapitation. This faradization evokes stepping in the hind-limb of that half of the cord to which the electrode (unipolar) is applied; and the ipsilateral stepping is often accompanied by weaker stepping of the contralateral hind-limb.

It appears clear, therefore, that the rhythmic response of the musculature is referable to a rhythm not resident in the stimulus or in sense-organs of the skin, but developed in the spinal centres occupied with the reflex action. In other words, in these centres there arises a rythmically recurrent refractory phase. Thus faradization of the cross-section of bulb or cord excites in the hind-limb of the same side a stepping movement which opens with limb-flexion; this flexion is succeeded a fraction of a second later by extension, this extension a fraction of a second late by flexion, and the flexion again by extension, and so on. In other words, the stimulus which primarily causes contraction of flexor muscles fails to do so a fraction of a second later, and then a fraction of a second later succeeds in exciting them again, and then again fails, and so on. The development of a refractory phase in reflex reactions is coming to be recognized as of common occurrence. The scratch-reflex, affecting as it does the same hind-limb muscles as does the reflex step, similarly exhibits a closely comparable refractory phase. In the scratch-reflex the tempo of the scratch-movement, *i.e.*, the rate of recurrence of the refractory phase, is little affected by alteration of the intensity of the stimulus. But in the stepping reflex, increase of the intensity of the stimulus increases the tempo of the step. This is equivalent to saying that intensifying the stimulus does not lead to prolongation of the excitatory effect; it brings increased intensity of discharge followed by acceleration of the onset of the refractory phase, and the refractory phase itself is of shorter duration.

The origin and intimate nature of the refractory phase is obscure. It is a phenomenon which seems akin in many ways to inhibition. Verworn and Fröhlich regard it as a relative exhaustion, a kind of fatigue. The well-known refractory phase of the heart during which the myocardium becomes irresponsive or incompletely responsive to stimulation naturally rises to mind as a possible type for a refractory phase in general. There is some evidence referring refractory phase in the heart to the liberation of potassium-ions present with sodium- and calcium-ions in the tissue.

And from the work of Macallum and of Macdonald we know the richness of the neuron in potassium and the intimate connexion between the liberation of this salt and functional activity. There is some evidence that the inhibitory action of the vagus on the heart is due to the liberation by that nerve of potassium from compounds that bind it in that part of the heart whence the beat originates. In the spinal reflexes under consideration the refractory phase is further complicated by the circumstance that these reflexes, step-reflex and scratch-reflex, are not only rhythmic but alternating. Thus, when the stimulus becomes ineffective for the flexor moto-neurons it becomes effective for the extensor moto-neurons, and conversely.

The stimuli above mentioned which excite stepping are all of them "*remote*"—that is, their place of application lies not within but outside the limits of the stepping limb itself. The stepping movement can, however, be excited by stimulation directly incident on the limb itself, though not by stimulation of its skin. Here the agent of stimulation has to be in the form of movement—for instance, passive movement of the limb. Perhaps posture also is effective. When the dog with spinal hind-limbs is lifted from the ground so that those limbs droop pendant, the hanging limbs at once begin to step. If, then, one of them be gently supported from beneath so that the hip is flexed, the reflex stepping subsides in it at once, and usually in the other limb as well, although that limb is quite free. On removing the support and letting the limb drop under its own weight once more, the passive extension so produced at once provokes active flexion at the crossed hip, and is followed in the limb dropped, after fair extension has occurred, by active flexion at the hip, the knee, and the ankle, accompanied in the fellow-limb by active extension at the similar joints. The stimulus exciting this reaction is the passive extension, chiefly of the hip. This reaction occurs just as well when all the skin-afferents of the limb are severed. The passive movement acts as a proprio-ceptive stimulus, and the reflex stepping as thus evoked is entirely a *proprio-ceptive reflex*.

An experiment of interest in this connexion is the following: The sartorius muscle (cat, dog) consists of two parts which form two parallel bands. Of these bands the median passes to tibia, and is a flexor of the knee as well as a flexor of the hip. The other passes to the patella, and is a flexor of the hip, but also an extensor of the knee, especially in its lower part. The sartorius can be separated from its insertions and its lateral and deep attachments without impairing its nerve or blood-supply. When this has been done it can be seen that in the decapitated preparation

passive full extension of the knee provokes reflex contraction of the median band of sartorius and in part of the lateral band; passive full flexion of the knee provokes reflex contraction of the lateral band of sartorius and, to a less extent, in the median band. Passive extension of the limb excites reflex contraction of a flexor of the limb, passive flexion of the limb excites reflex contraction of an extensor of the limb. But of the two effects, the former is the more marked and regular in the decapitated preparation. This applies also to other flexor muscles. Thus passive extension of the knee and the ankle, and of the knee alone, excites reflex contraction in the semitendinosus and biceps femoris posterior—both of them flexors of the knee. But the same passive extension does not excite contraction in the semimembranosus or biceps femoris anterior, extensors of the hip and indirectly of the knee.

Such results are evidently akin to the phenomenon of *reversal*, the observation of which we owe to J. v. Uexküll and R. Magnus. This *reversal* consists in a reversal of the direction of a reflex movement brought about by reversing the initial posture of the joint or joints affected by the reflex. Thus, in the ray-arm of the brittle-star (v. Uexküll) and in the tail of the spinal cat (Magnus) the stimulus which, when the initial pose of the appendage is to the left deflects it to right, deflects it to left when the initial pose is to the right. Magnus has shown that a similar influence is traceable in the spinal reflexes of the dog's hind-limbs. From such "reversal" influence it seems only a step further when, as in the above experiments, a passive extending of the knee excites, towards its completion, a reflex contraction of the knee-flexors.

But in my experience, so far as it goes, movements of a purely passive kind do not excite reflex movement of opposite direction to their own with that readiness which might be expected were they of themselves alone wholly competent to give the alternations exhibited by such reactions as the step-reflex and the scratch-reflex. It would seem that additional factors must co-operate in the production of these alternations. And these additional factors may be present in active movements, though wanting in movements merely passive. In the active movement not only are the muscles antagonistic to the movement lengthened passively by the mechanical pull of the movement, but they are relaxed by central inhibition of their excitation of whatever grade that may be at the time. And in addition their protagonists, the prime movers, as Charles Beevor, whose loss is still so fresh a grief with us, termed them, are shortened and tightened and subjected to electrical disturbance—in short, become seats of change they do not experience in merely passive movement.

Active movements appear competent, therefore, to originate proprioceptive stimuli more potently than passive movements. And Goldscheider found their threshold of perceptibility lower, though not greatly lower, than that for passive movements. If they are more potent exciters of sense they may be expected to be more potent exciters of reflex action. And, further, an active movement predicates active changes excitatory, and inhibitory, in the spinal centres themselves, and of a kind and in a measure wanting to purely passive movements. In these active *central* changes, excitatory and inhibitory, seems to lie an important predisposing condition for further changes determining subsequent reflex events.

To consider these it is necessary to revert for a moment to the actual distribution of the reflex effect upon the limb-musculature observable in each of the two phases which compose the limb-movement of the reflex step. The step is a diphasic movement. There is a flexion phase in which the limb, its weight being carried as Weber showed by the atmospheric pressure on the hip-joint, is drawn forward by flexion at the hip, and is lifted clear of the ground by flexion of the knee and ankle during the earlier two-thirds of the phase. On the flexor phase follows the extensor phase. In this phase the hip, knee, and ankle are simultaneously extended, and the straightening limb propels the body forward at the same time supporting its weight.

In this diphasic movement the protagonists of one phase are the antagonists of the other. Thus such a muscle as the vastocrureus is a protagonist in the extensor phase, and as such exhibits excitation during that phase. But in the flexion phase, where for instance the sartorius is a protagonist, the vastocrureus is an antagonist, and as such exhibits inhibitory relaxation. In each of the two opposed phases certain motor neuron-groups are being excited, and certain concurrently depressed by inhibition. And the groups depressed by inhibition are the antagonists of the groups which are excited. Thus, the extension phase of the step is brought about by excitation of the extensor centres of the limb with concurrent inhibition of the flexor centres; and the flexion phase of the step is brought about by excitation of the flexor centres and concurrent inhibition of the extensor centres. Now a common phenomenon when reflex flexion of the limb is produced in the spinal, and especially in the decerebrate, preparation, is that on withdrawal of the stimulus producing the flexion, not merely does the flexion lapse, but it is followed by an active extension. This *rebound* extension appears due to a post-inhibitory exaltation of activity in the previously inhibited

extensor centres. Conversely a rebound flexion often ensues on withdrawal of a stimulus excitatory of extension. These rebound discharges are akin to a phenomenon which Head [3] noted in his work on the regulation of the respiratory movements. Head stimulated the central end of one vagus with faradic currents just too weak to produce a

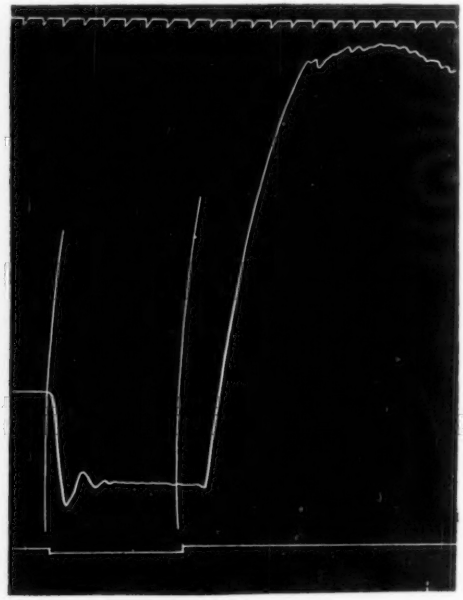

FIG. 1.

Post-inhibitory exaltation. The tracing is from the knee-extensor, *vastocrureus*. The muscle is at the outset of the tracing exhibiting tonic contraction, for it is taking part in the postural reflex of standing which involves maintained extension of knee. A stimulus is then applied (*see* notch in signal line below) appropriate for producing knee-flexion. The vastocrureus is immediately relaxed (descent of myograph line) by reflex inhibition, and remains relaxed so long as the stimulus continues. The stimulus is then withdrawn and the muscle re-exhibits contraction (rebound contraction), and this contraction is greatly in excess of the grade of the contraction it exhibited prior to the reflex inhibition. Time in quarter seconds above.

complete reflex tetanus of the diaphragm. During this condition an inflation of the lung at once produced relaxation of the diaphragm by reflex inhibition. When the lungs had returned to their normal volume after the inflation, the stimulus previously inefficient to produce complete tetanus of the diaphragm became at once efficient. A period

of inhibitory depression is followed by a period of increased responsiveness to excitation. Similarly, with the spinal limb-centres a stimulus evoking only a slight reflex extension of the limb will, when applied soon after the occurrence of a strong flexor reflex of the limb, evoke a much more ample and long-lasting reflex extension than

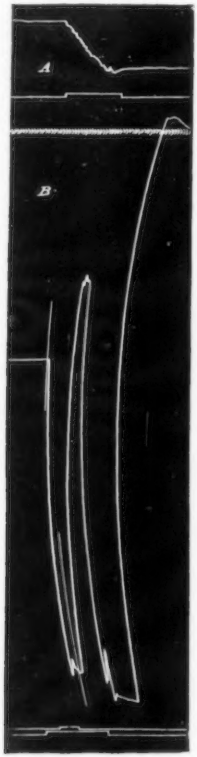

FIG. 2.

Post-inhibitory exaltation. Tracing from the knee-extensor, *vastocruræus*. A, exhibits the weak reflex inhibition caused by a weak stimulus. B, powerful reflex inhibition caused by a much stronger but otherwise similar stimulus. This stimulus for the period shown by the rise in the upper signal line in the lower tracing was abruptly weakened to the lesser intensity it had in A. The muscle under this change at once reverts to contraction not merely of the grade that it had before the inhibition, but to a higher grade of contraction than that. Post-inhibitory exaltation has so heightened the activity of the reflex centre that a rebound contraction occurs in spite of the weak inhibitory stimulus which previously was able to produce distinct relaxation of the muscle. On restoring the full intensity of the inhibitory stimulus full relaxation returns once more. On withdrawing the inhibitory stimulus altogether a final rebound contraction occurs exhibiting still more marked post-inhibitory exaltation. Time in quarter seconds.

it did before [8]. In the decerebrate preparation the reflex inhibition of an extensor muscle is followed on removal of the inhibitory stimulus by a seemingly spontaneous rebound contraction of the muscle [9]. (Figs. 1 and 2.) This rebound is obtained even when all other nerves of the limb have been severed, except only that of the extensor muscle itself. It is, therefore, not necessarily dependent on the movement produced by the precurrent flexion-reflex, for, although the stimulus which inhibits the extensor muscle would produce the flexion-reflex were the limb musculature intact, the musculature having (except for the extensor muscle in question) been entirely paralysed by nerve-section, the flexion movement cannot take place. The rebound appears, therefore, of *central* origin. It is a sign of the exaltation of activity which commonly follows inhibition. But that that exaltation culminates in actual spontaneous discharge from the centre under rebound is doubtful. The post-inhibitory contraction of the extensor is probably a return in exaggerated measure of the tonic contraction of the extensors (antigravity muscles) usual in the decerebrate preparation. That tonic contraction is reflex, and due to a stimulus of proprio-ceptive kind. It is inhibited by the stimulus which causes the flexion phase of the step, and returns on withdrawal of that stimulus, and its exaggeration on return merely means that the proprio-ceptive stimulus which produces it finds the responsiveness of the extensor centres heightened after the temporary period of inhibition. The phenomenon is, therefore, simply another item of evidence that a *post-inhibitory exaltation* of spinal activity occurs in the nervous centres of the limb.

We may now attempt in the light of the above facts to trace the manner of production of the stepping reflex as excited by one or other of the various stimuli which evoke it from the skin of the decapitated preparation. These stimuli are remote, and they are of noxious character. In these respects they contrast with the intrinsic stimuli, *i.e.*, the stimuli which excite the reflex when applied to this stepping limb itself. These latter are not cutaneous, and are innocuous and proprio-ceptive. Part of the problem pertaining to the reflex step lies in harmonizing the two sets of stimuli so widely different. We may take the case of a continued stimulus, *e.g.*, pressure or faradization applied to the skin of one hind-limb exciting reflex stepping in the other hind-limb. The stepping movement begins with active extension of the limb. It was shown that passive extension of the limb tends to excite an active reflex flexion of the limb, and does so by generating in the

deep structures of the limb a stimulus which excites reflex flexion. In short, the primary remote stimulus, noxious and cutaneous, reflexly provokes an extension-movement of the limb, and this movement generates in the extending limb a secondary and proprio-ceptive intrinsic stimulus whose reflex effect on the limb is antagonistic to that of the primary stimulus. Thus arises a competition between two stimuli whose influences on the motor neurons of the limb are directly opposed one to the other. If the secondary stimulus prove strong enough there will ensue flexion of the limb in spite of the continued application of the primary stimulus. But with the occurrence of flexion the secondary stimulus will diminish and the primary stimulus will again assert itself, reinforced probably by a tertiary proprio-ceptive stimulus generated in the limb by the flexion of the limb and tending to produce extension. Extension therefore recurs and the process repeats itself as before. And in each of these changes from extension to flexion, and especially from flexion to extension, post-inhibitory rebound facilitates the change. Indeed, the burden of shunting from flexion to extension and *vice versa* is thrown greatly upon mechanisms wholly intrinsic to the cord. But the interference between the local proprio-ceptive stimulus and the remote continuous stimulus *regulates* the tempo at which the alternation, the shunting, proceeds.

A similar description applies conversely to the case where the remote stimulus, *e.g.*, faradization of the cross-section of the cord in the first cervical segment excites stepping of the ipsilateral hind-limb with flexion as the opening phase of the step. Here we may consider that we have a continuous stimulus to flexion broken in its operation recurrently and rhythmically by a local proprio-ceptive stimulus to extension, this latter secondary stimulus being engendered in the limb by the movement of flexion which the primary stimulus evokes. Here, again, the change from flexion to extension and conversely is facilitated by post-inhibitory rebound, of the inhibited extensor centres after flexion, of the inhibited flexor centres after extension.

And to this mechanism, and when the stepping is bipedal and involves *both* hind-limbs, must be added an adjuvant influence from the fellow hind-limb. The hind-limbs of the spinal dog show that when the initial posture of one hind-limb is flexion at hip and knee and of the other extension at those joints, on allowing the flexed limb to drop into extension the opposite limb at once flexes at hip and knee. And directly full extension is reached by the dropped limb active flexion occurs in it and is accompanied by active extension of the opposite hip and knee

that have just previously flexed. This crossed reflex influence reinforces the mechanism producing the alternations of extension and flexion in the fellow-limb; it is so potent in some cases that arrest of the stepping in one limb soon causes cessation of the stepping in the other limb also. And this crossed influence is an important factor in keeping the phases of the stepping in walking and trotting correctly timed though converse in phase in the two limbs, right and left.

The experimental results in regard to reflex stepping point, therefore, to a mechanism comparable with that of the "Selbsteuerung" of the inspiratory movement discovered by Hering and Breuer[1] [4]. There it was shown that the contraction of the diaphragm in inspiration is in due course cut short by a reflex inhibition, traceable to a stimulus generated by the mechanical stretch which the inspiratory movement itself produces in the lungs, also by that of the diaphragm itself (Baglioni [1]). The inspiratory reaction is therefore arrested by a secondary reflex of its own making, a secondary reflex antagonistic to the primary reaction in regard to its influence on the respiratory muscles. Similarly in the case of the vasomotor centre and the heart, intense action of the general vaso-constrictor centre, by raising the aortic blood-pressure, stretches the aortic wall, and by so doing excites the afferent nerve of the aorta,[2] *n. depressor*, and through it reflexly depresses the action of the vaso-constrictor centre.

In these cases the primary reaction generates a secondary one antagonistic to the primary itself. Thus during reflex stepping a conflict recurs rhythmically between two stimuli of opposed influence on the limb musculature, or rather on the motor neurons of that musculature, one stimulus exciting the extensor motor neurons and inhibiting the flexor, the other inhibiting the extensor and exciting the flexor. The case of the concurrence of two stimuli having opposed influence on the motor neurons of one and the same field of musculature has been examined [10] for muscles which the reflex step actually engages—namely, those of the knee. The result of the competition between the opposed influences is found to fall into one or other of three types, according to the relative intensities of the opposed stimuli. (Figs. 3 and 4.) If A is a stimulus exciting motor neurons E and inhibiting motor neurons F, and if then a stimulus B arise whose influence is to inhibit motor neurons E and excite motor neurons F, the three types of result, as actually

[1] Also Head [3], Gad [2], Lewandowsky [5].
[2] A. Tschermak and G. Koster [11].

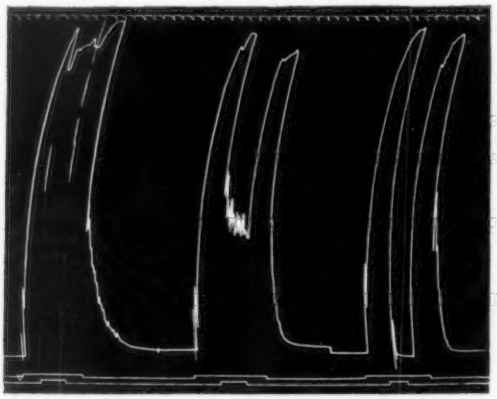

FIG. 3.

Reflex contraction of *vastocrureus* in spinal mammal (decapitated cat), excited by faradic stimulation of contralateral popliteal nerve (C). During this contraction the ipsilateral peroneal nerve was faradized for the time shown by the lower signal (I), and produced a lessening of the reflex contraction; this inhibitory effect is greater according as the intensity of the stimulation of the ipsilateral nerve is increased. In the second observation it reduces the reflex contraction to less than half; in the third observation it suppresses it altogether for so long as the inhibitory stimulus endures. In the third observation, with the strong inhibition, so abrupt and quick is the suppression of the contraction that the writing lever gives a vibratory shake at the end of its fall. The tremor seen to occur in the second observation during the period of concurrent excitation and inhibition is usual, and is more marked in the decapitated preparation than in the decerebrate. Time in seconds above.

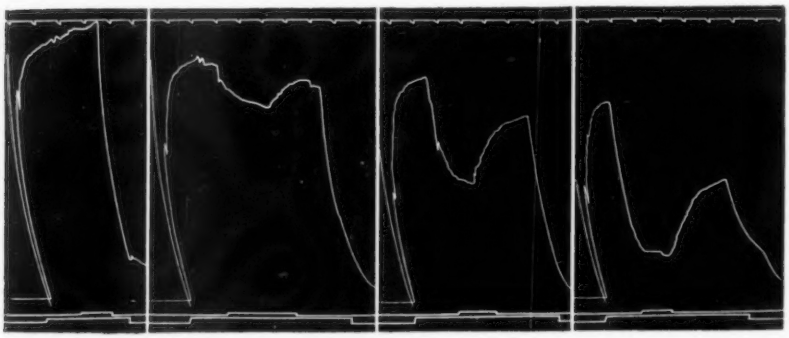

FIG. 4.

Reflex contractions of semitendinosus, a flexor of knee, evoked by stimulation of ipsilateral peroneal (I) nerve; the contraction is inhibited in each observation by an intercurrent stimulation of the contralateral popliteal nerve (C). The intensity of the ipsilateral stimulus—the excitatory—is progressively lessened from observation I to observation IV, while the intensity of the inhibitory stimulus (C) is kept the same for all the observations. Cat, decerebrate preparation. Time in seconds above.

observed, are as follows: If B is much weaker than A its inhibitory influence is unable to modify perceptibly A's excitatory influence, and A's inhibitory influence wholly prevents B's excitatory effect from showing on the muscle. If B is much more intense than A, B's excitatory effect wholly overcomes A's inhibitory effect, to judge by the muscle, and B's inhibitory effect wholly suppresses A's excitatory effect. If A and B are of not very unequal intensity the excitatory effect which A is producing is partially suppressed by the inhibitory influence exerted by B, and the inhibitory effect which A is producing only partially suppresses the excitatory influence which B brings to bear. In other words, there results a contraction, both of the muscles E which A excites and of their antagonists, the muscles F, which B excites, but the contraction of E is less than it was when A was acting alone, and the contraction of F is less than it would be were B acting alone. In short, *double reciprocal innervation* is at work and the results of stimulus A and stimulus B sum algebraically in their effect, both on muscle E and on muscle F.

In the case of the reflex step, therefore, when the stimulus S, by its reflex effect on the limb-muscles, generates in the limb a local stimulus S′ antagonistic to S itself, the exact effect on the limb musculature depends on the relative intensities of S and S′. When the stimulus S is very intense as compared with S′, as is the case when a noxious stimulus is applied to the skin of the limb itself, S′ is unable to modify the effect of S, and the usual nociceptive unalternating reflex results, the protective reflex folding up the limb out of harm's way. When S is remote, and, therefore, as regards its efficacy on the distant limb, less intense, the intensity of S′ is sufficient to interfere with the effect of S, and the rhythmic alternating reflex, stepping, ensues. But it remains a question in any particular case whether the intensity of S′ is sufficient temporarily to suppress S's effect wholly or only in part. If the latter, and taking the case of S's effect being flexor, the flexor movement will change to extensor movement when S's influence arises; the flexors will, under that influence be partially relaxed and the extensors will concurrently contract to some extent. My impression is that in many instances the reflex stepping of the decapitated preparation belongs to this form; *i.e.*, that the relaxation of the relaxing muscles is partial, and does not extend to complete suppression of all contraction, and similarly that the contraction of their opponents does not reach its maximum extent. This impression is strengthened by the analogous scratch-reflex, in which, in many instances, it can be seen that the rhythmic clonus is due to

partial relaxations of a persistent contraction maintained throughout the reflex. Similarly, when the respiratory movements are quick and deep, the contraction of the diaphragm does not wholly cease during expiration: the diaphragm relaxes, but its relaxation is only partial. In the stepping of the decapitated preparation there is evidence that the effect of the remote nociceptive stimulus preponderates over that of the intrinsic proprio-ceptive stimulus. The former stimulus, when its locus of application lies in the median line of the perineum, causes a bipedal stepping which is remarkably similar in form in the two limbs right and left. But if the point of application of the stimulus be shifted somewhat to the right, the stepping of the right hind-limb, although its tempo is not altered, is characterized by greater flexion, especially at the hip, while that of the left limb, without alteration in tempo, becomes characterized by greater extension, especially at the hip. Now the stepping initiated from the base of the ipsilateral limb opens with flexion, while that initiated from the crossed limb opens with extension; in short, the remote stimulus is responsible in the ipsilateral limb for flexion, in the crossed limb for extension. It is clear, therefore, that in this case of reflex stepping the remote or initiatory stepping predominates over the intrinsic or secondary stimulus in each limb. And it is also clear, from this and other observations, that the exact form assumed by the reflex stepping of a limb is largely governed by the nature (locus, &c.) and intensity of the remote stimulus in relation to the secondary intrinsic one. By grading the rhythmic partial relaxations due to graded intensities of the two opponent stimuli S and S′, various forms can be given to the reflex step. Whether under the competition between the remote primary and the intrinsic secondary stimulus the third form of result ever ensues remains without direct answer from my observations. My impression is that, in the case of the more perfect reflex stepping of the spinal hind-limbs of the dog, after the period of shock has passed, it can be seen to occur. When that stepping is slow and ample, as it sometimes is, my impression is that flexors and extensors may fully relax alternately: just as in natural breathing the diaphragm may, for a short time, during the expiratory phase, show a complete absence of contraction.

As to the tempo of the stepping, a factor largely governing it is clearly the intensity of the remote initiatory stimulus. With increase of stimulus S the tempo of the step is quickened. This is well seen when the hind-limb stepping is excited by faradization of the cross-section of the bulb or cervical cord. Increase in the intensity of the stimulus does not prolong the excitatory effect: it gives an increased intensity of

discharge followed at increased speed by a refractory period and alternation of phase, these latter also of shorter duration. Such a result harmonizes well with the view put forward by Verworn and Fröhlich as to the nature of refractory phase and inhibition.

It seems permissible to draw one conclusion from the experimental observations on reflex stepping at least in regard to stepping as naturally executed under the initiation of the higher centres, let us say although the expression has but vague connotation in physiology, under the mandate of the will. The inference from the experiments is, that in such a case the excitatory influence descending from the higher centres to the spinal centres of the limbs is not an intermittent periodic one whose periods determine the periods of the sequence of the steps, and still less does it consist of two alternating periodic influences—one determining the recurrence of one phase of the step, the other determining the recurrence of the other phase of the step. The excitatory influence descending to the limb centres is a continuous one, whose continuous operation is in a rhythmic manner completely or partially interrupted by an antagonistic reflex reaction secondarily generated in the limb. And when the continuously descending excitatory influence is intense, it provokes quicker steps than when it is less intense.

But the decapitated preparation, though it can perform stepping movements with its limbs, cannot effectively walk or run. The stepping of its fore-limbs is, in my experience, less easy to provoke and less perfect than in the hind-limbs. But there are other reasons also for its inefficiency as regards actual progression. One of these is its inability to support the erect posture. It cannot stand. The decerebrate preparation is less readily excited to step, but its stepping, when elicited, is much more effective and amounts in many instances to actual though imperfect progression (cat). Between reflex standing and reflex stepping the nexus is natural and close. The reflex stepping, when evoked in the limbs of the decerebrate preparation, clearly appears as a series of reflex flexions of each limb in turn breaking through the static postural reflex of standing and followed in each limb in turn by a return of the static reflex in exaggerated measure. The extensor phase of the step is much stronger in the decerebrate preparation than in the decapitated. An inference is that in the decerebrate preparation the same pre-spinal mechanism, in virtue of which the preparation can stand, contributes also to the extensor phase of the step. Probably it is shock consequent on loss of this pre-spinal mechanism which makes extensor-reflexes usually less easy to evoke than flexor in the decapitated preparation, and causes

them to recover later in the spinal limbs after thoracic transection. It seems unnatural that experimental records in these "acute" preparations—the decerebrate and the decapitated—should find reflex stepping obtainable as a purely spinal reaction, while reflex standing is only obtainable where the hind-brain and part of the mid-brain remain in addition to the spinal cord. The answer seems to lie in the circumstance that the latter, the postural reflex, is an extensor reflex, whereas the former is only partly an extensor reflex and depends also on flexor mechanisms, and these mechanisms suffer less than extensor from removal of the pre-spinal centres so greatly adjuvant to the latter. In the frog, where the habitually resting posture on land is with hind-limbs flexed, the spinal preparation preserves well that reflex posture of the hind-limbs. The postural tonus of the hind-limbs of the frog is a flexor tonus, and the Brondgeest experiment shows the tonus there to be a static reflex dependent on the afferents of the limb; Bernard's observations showed, further, that the afferents involved are not those of the skin of the limb, but those of the deep structures. In short, like the standing posture of the hind-limb of cat and dog, it is a proprio-ceptive reflex from the limb itself.

The decerebrate preparation retains the reflex mechanisms for executing stepping movements, and also for supporting the erect posture; yet it is not very readily driven to exhibit reflex walking and running. To elicit locomotion in it the stimuli have to be intense, and such as are of a nature to evoke pain, did consciousness exist in the preparation. And with the locomotor movements thus initiated go pseudo-affective movements [12] of face and larynx suggestive of defence as well as flight. We may ask, what is the reason of this want of readiness of locomotor response in a preparation that still possesses so much of the neuro-muscular apparatus subserving such response? Is it because the intercollicular transection, by cutting off the great distance-receptors for olfactory, optic, and to a great extent acoustic stimuli, and all the superstructure concerned with sensuous elaboration of fillet impulses, has so reduced the creature's responsiveness that the mere static proprio-ceptive reflex of quiescent posture can engage it undisturbed? Has its world petrified to a motionless system, wholly static, an invariant monotone bereft of all symbolism of change? Has the mutilation involved removal of some nodal region habitually initiatory of progression? In absence of that focal region has it become difficult even for afferent channels still remaining to the

creature to unify its reactions into so complex and wide a motor response as that involved in progression?

The observations of Goltz, and more recently of Rothmann, have shown that the dog, deprived almost wholly of both cerebral hemispheres, can stand and walk. Goltz's dog would, when feeding time approached, rear itself so as to rest its fore-paws on the gate of the kennel. In its roaming, it on one occasion wounded its hind-foot. It was then observed to walk on three feet, holding the injured foot off the ground. In even the decapitated preparation (cat) a somewhat similar reaction can be seen. If, as the preparation lies on its side, one hind-foot be forcibly pinched, this limb is flexed at the hip, knee, and ankle, and the other limbs at once begin rapid, co-ordinated stepping movements. The injured foot is held up out of harm's way, and the other legs run away.

Even in such a high animal type as the dog the whole complex act of reflex progression can therefore be performed not only without the collaboration of the cerebral cortex, but also in practical absence of the whole cerebral hemispheres themselves. That the posterior thalamic region is of importance in this connexion is indicated by the observations of several observers, and notably of Thiele. The red nucleus probably also contributes, as its recent analysis by v. Monakow indicates. The experiments of Horsley and of Thiele show that decerebrate rigidity is hardly seriously impaired by successive sections of the cerebellar region until the paracerebellar nuclei are invaded. In this problem of co-ordination, as in so many others, the justice and penetration of views long expressed by Hughlings Jackson meets us. More than thirty years ago Jackson wrote laying stress on the importance of the distinction between "continuous movements" and "changing movements." "In walking the cerebellum tends to stiffen all the muscles; the changing movements of walking are the result of "discharges overcoming in a particular and orderly way the otherwise continuous cerebellar influence." Under experimental procedure the two reflex elements, the static of erect posture and the kinetic furnishing rhythmic alternating movement of the stepping limbs, disengage themselves as separable components of the total reflex of progression. How exactly they are combined in such an act as walking remains for further elucidation, and we must, I think, for the present leave them with that question unanswered; the information before us seems still insufficient to solve the problem.

But we may glance back finally at the above component reflexes

used in progression to look at certain principles of simpler co-ordination which they exhibit in their handling of the musculature of the limb. To take first the rhythmic diphasic motion of the limb which constitutes the step. It has already been mentioned that the muscles which are protagonists in the one phase are not so in the other; the protagonists of one phase are the antagonists of the other. And this is true equally for both phases. It is well seen when the musculature of the limb is analysed in regard to the part played by its several muscles individually in the respective phases of the step. In each phase certain muscles are found to be contracting and certain to be relaxing. In the flexion phase (fig. 5, A), the muscles which after appropriate isolation can be detected to be actually shortening by active contraction are *psoas*, *sartorius* (except perhaps lower part of lateral band), *rectus*, *gracilis*, *biceps femoris posterior*, *semitendinosus*, *tibialis anticus*, *extensor longus digitorum*, *peroneus longus*, *gluteus minimus*, and *tenuissimus*. On the other hand, certain muscles can similarly be detected actually to relax in this phase. These are: *semimembranosus*, *biceps femoris anterior*, *quadratus femoris*, *vastus lateralis*, *vastus medialis*, *crureus*, *adductor minor*, *gastrocnemius* and *soleus*. That these muscles relax during this phase of the step does not necessarily mean that they relax to such a degree that no contraction remains in them. It merely means that the grade of contraction which they exhibit at the outset of the phase lessens during the phase. The extent to which their pre-existing contraction relaxes is proportioned to the degree to which the contraction of the opposing muscles is augmented. And the relaxation is brought about by reflex inhibition of the centre innervating them, just as the augmentation of the contraction of the opponent muscles is due to reflex excitation of the centre innervating those muscles. MacDougall's drainage-theory very aptly expresses this result. Evidently the principle exhibited by the taxis of the reflex in handling these protagonists and antagonists is that of reciprocal innervation. It does not at all preclude the co-existence at one and the same time of a certain amount of active contraction in both protagonist and antagonist. What it does preclude, and what does not in fact appear ever to occur, is concurrent increase of contraction in both protagonist and antagonist, and concurrent decrease of contraction in both protagonist and antagonist. When excitation of the flexor motor neuron is being augmented by further excitation, that of the extensor motor neuron is by inhibition being correspondingly lessened: and conversely.

In the extension-phase of the step (Fig. 5, B) the following muscles

are by analysis found to be contracting: *quadratus femoris, biceps femoris anterior, semimembranosus, vastus lateralis crureus, vastus medialis, adductor minor, gastrocnemius, soleus,* and *flexor longus digitorum.* The muscles observed to relax in this phase are: *psoas, sartorius, rectus femoris gracilis, semitendinosus, biceps femoris posterior, gluteus, minimus, tibialis anticus,* and *extensor longus digitorum.* In this phase, also, protagonists and antagonists are dealt with by reciprocal innervation.

Reference to the above lists, and to the accompanying diagram (fig. 5) illustrating them, shows, however, that in each phase of the step

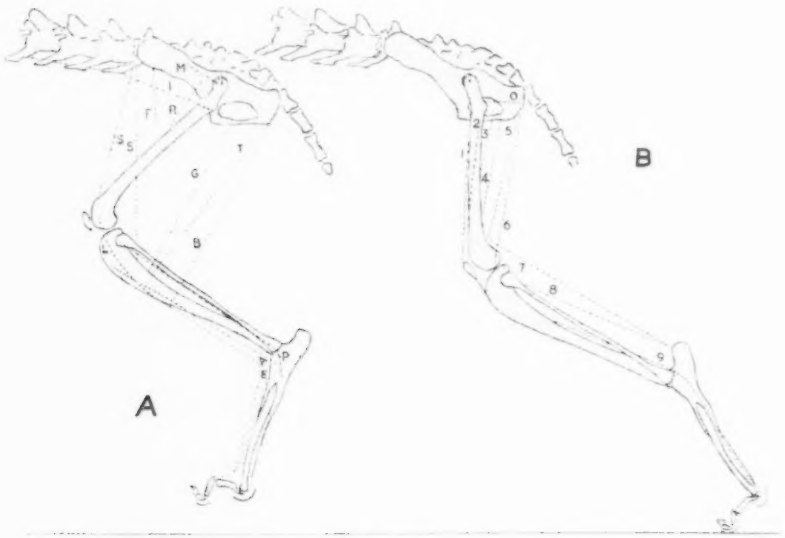

FIG. 5.

Figure illustrating the muscles actually observed by experimental analysis to be engaged in contracting in the flexion-phase A and in the extension phase B of the reflex step of the cat.

A.

A, tibialis anticus.
B, biceps femoris posterior.
E, extensor brevis digitorum.
F, tensor fasciæ femoris brevis.
G, gracilis.
I, psoas.
L, extensor longus digitorum.
M, gluteus minimus.
P, peroneus longus.
R, rectus femoris.
S, sartorius lateralis.
S', sartorius medialis.
T, semitendinosus.

B.

0, quadratus femoris.
1, crureus.
2, vasti.
3, adductor minor.
4, adductor major (a part).
5, semimembranosus.
6, biceps femoris posterior.
7, gastrocnemius.
8, soleus.
9, flexor longus digitorum.

certain muscles which, in a sense, are antagonistic to each other, are not dealt with by reciprocal innervation. That is, certain muscles which oppose each other's action are identically innervated, *i.e.*, are together excited to contraction, and are inhibited together and at the same time. A good example is that of the semitendinosus or biceps femoris posterior, along with the psoas or sartorius. The two former muscles are flexors of knee and also extensors of the hip; but though extensors of the hip they contract during the flexion-phase of the step when the hip is being flexed. The extension of the hip which they tend to produce is wholly prevented and overcome by the concurrent contraction of the psoas and sartorius (mesial band), which are in so far their antagonists. But this prevention of their mechanical effect at the hip enhances their flexor-effect at knee. Hence it is clear that the reflex taxis is such that the hip flexors, whilst protagonists of flexion at that joint, serve also as fixators for the protagonist flexors of the next joint, the knee. The reflex taxis employs the same muscles as protagonists at one joint, and as fixators for the protagonists of the next joint. This is a principle commonly to be observed in the reflex movements of the limbs in cat and dog. The reflex makes certain muscles, which in H. E. Hering's term are pseudo-antagonists, synergic with the protagonists for the sake of fixation of adjacent joints. These muscles, along with the protagonists it deals with by identical innervation, not by reciprocal innervation.

A similar case is that of gastrocnemius. In the extension phase of the reflex step this muscle contracts; it extends the ankle, and if acting by itself alone would flex the knee. But the reflex taxis is such that the muscle's flexor action at the knee is prevented. The knee extensor, vastocrureus, is thrown into contraction concurrently with the gastrocnemius. The vastocrureus, by preventing the gastrocnemius from flexing the knee, enhances the latter's action as an extensor of ankle. Again, when the ankle is flexed in the flexor-phase of the step, not only is the gastrocnemius the direct antagonist of the ankle-flexors relaxed by reciprocal inhibition, but so, likewise, is the vastocrureus. This last, on account of the origin of the gastrocnemius above knee-joint, is an indirect extensor of ankle. Vastocrureus and gastrocnemius, although partial or pseudo-antagonists, are by the reflex taxis made synergic and handled by identical innervation.

If we turn to the static reflex of standing, as exemplified by the purely reflex standing of the decerebrate preparation, we find in this postural reflex also the same principles observed as in the kinetic reflex

of the step. Thus the protagonists which keep the knee extended are here, as in the extension phase of the step, the vasti and crureus. Main antagonists to these are semitendinosus, biceps femoris posterior, sartorius (medial band) and gracilis. In these antagonists, while their protagonists remain in steady tonic contraction, observation fails to show any contraction; on the contrary, it finds them under a slight degree of inhibitory restraint, the converse of the protagonist's degree of reflex excitation. Here, apparently, the static reflex, like the kinetic, deals with protagonist and antagonist by reciprocal innervation. The muscles which appropriate experimental analysis finds to be exhibiting tonic contraction in this postural reflex are the following: *quadratus femoris, semimembranosus, biceps femoris anterior, vastus lateralis, vastus medialis, crureus adductor minor, soleus* and *gastrocnemius;* probably also flexor longus digitorum, though in this last the tonic contraction is slight. And, here again, it is obvious that certain of the muscles exhibiting contraction simultaneously are nevertheless to some extent opponents of each other's action. Thus the gastrocnemius and vastocrureus are opponents in respect of their action at knee. Yet the reflex taxis makes them synergic muscles. And with the same result as in the kinetic reflex of the extension-phase of the step: the vastocrureus, by opposing the flexor action of the gastrocnemius at the knee, enhances the extensor action of that muscle at the ankle. These pseudo-antagonists are dealt with by identical innervation, not by reciprocal innervation, as are the true antagonists.

Finally, it may be remarked that the reflex taxis both of the step and of standing in many cases does not treat as functional units certain items of the musculature regarded as unit muscles by anatomical nomenclature. Thus it deals with the biceps femoris as a double muscle compounded of a pair of units, which have the mutual relation of protagonist and antagonist. The portion of the muscle which is inserted above the knee-joint it treats along with the extensors of the limb, that portion inserted below the knee-joint it associates with the flexors of the limb. Hence, in the account given above, a biceps femoris anterior has been distinguished from a biceps femoris posterior, because these are functionally dealt with by the reflex as two separate muscles. Similarly the reflex treats that part of quadriceps extensor which constitutes the rectus femoris as a flexor, while the rest of the quadriceps it relegates to the extensor mechanism of the limb. When the distribution of the knee-jerk in the muscular field of the limb is examined, one part of quadriceps is found to be unoccupied in the jerk-reaction—

that part is rectus femoris. This is undoubtedly connected with the circumstance that the reflex machinery of the limb treats the rectus as a flexor. It would seem that the jerk phenomena are all confined to those groups of muscles which were referred to as "anti-gravity" muscles, the muscles which by their contraction counteract gravity in the usual erect posture, the ususstatus, of the animal.

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"A CONTRIBUTION TO THE LOCALIZATION OF CEREBRAL FUNCTION, BASED ON THE CLINICO-PATHOLOGICAL STUDY OF MENTAL DISEASE."[1]

BY JOSEPH SHAW BOLTON, M.D., F.R.C.P.

CHAPTER I.—General Remarks on Cortical Localization.
CHAPTER II.—Method of Investigation.
CHAPTER III.—The Lamination of the Normal Cortex and its Mode of Evolution.
CHAPTER IV.—The Lamination of the Visuo-sensory Area, the Visuo-psychic Zone, and the Prefrontal Region.
CHAPTER V.—Intracranial Abnormal and Morbid Appearances in Mental Disease. Generalization of Amentia and Dementia.
CHAPTER VI.—Micrometric Examination of the Cerebral Cortex in Mental Disease.
CHAPTER VII.—The Pre-Rolandic or Psychomotor Cortex.
CHAPTER VIII.—Provisional Scheme of the Localization of Cerebral Function.
CHAPTER IX.—The Nature of Language, and the Language Mechanism.
CHAPTER X.—Defective Control of Processes of Lower Association in Mental Disease.
CHAPTER XI.—Independent Activity of the Centres of Lower Association.—Illusion and Hallucination.
ADDENDUM.
APPENDIX A.
APPENDIX B.

MR. PRESIDENT AND GENTLEMEN, in thanking you for the honour you have done me by your invitation to deliver the Goulstonian Lectures for the present year, I wish at the same time to apologize for my presumption in choosing as my subject such a vexed and intricate question as the localization of cerebral function. I have but one excuse to offer—namely, that in my researches I have attacked this subject by a somewhat different method from any hitherto adopted, and have thereby obtained results which appear to me partly to confirm and partly to amplify the conclusions arrived at by certain other and more experienced workers. As my present investigations have already occupied a considerable period of time, it being now fourteen years since their commencement, and ten years since my first paper on cortical localization was published, I think I may fairly claim that the conclusions at which I have arrived are neither hasty nor ill-considered, and I therefore trust

[1] The Goulstonian Lectures delivered before the Royal College of Physicians of London on March 1, 3, and 8, 1910.

that you will regard these, and also the evidence which I am about to lay before you, as not entirely unworthy of your attention.

Chapter I.

General Remarks on Cortical Localization.

I do not propose to enter into a historical retrospect of the investigations of the past forty years, as for my purpose it is sufficient to refer briefly to those of the past decade. With regard to the earlier researches, I would remark that the experimental method of investigation which was introduced by Fritsch and Hitzig and by Ferrier, and continued by numerous workers, from whose names it would be invidious to make a selection, may be considered to have served its purpose with the publication of the researches of Sherrington and Grünbaum [19]. These, by linking together the conclusions arrived at by the experimental and the histological methods, resulted in the belated recognition of the neglected histological investigation of Bevan Lewis and Henry Clarke [16] on the cortical localization of the motor area, and gave an impetus to the latter method which has already been followed by a considerable amplification of our knowledge of the structure and functions of the cerebrum.

The last, but not the least important, of the researches to which I must refer before dealing with the published work of the past few years are those of Flechsig [11] on the development of the human brain by a study of the process of myelination. The division of the cortex cerebri, by this investigator, into the two great classes of "sensory centres" and "centres of association" raised a storm of discussion and dissent which is almost unprecedented in the history of research, and which, but for Flechsig, would have overtaken the workers of the past decade. Though many of the results obtained by Flechsig have failed to obtain credence, largely perhaps through the frequency with which he modified them in successive publications, his broad generalization has successfully withstood the fire of criticism, and forms the origin, if not entirely the basis, of our present knowledge of cortical localization by histological methods. In my personal opinion, which is based on my experience of the great differences which exist in the degree of development of fœtal and infantile brains of approximately the same age, Flechsig was injudicious in applying directly to the adult cerebrum the results he obtained from the investigation of such brains; but it is easy to be wise after the event, and it is probable that the

researches of Flechsig would have attracted less attention had they excited less dissent.

During the past decade numerous publications have appeared on the subject of cortical localization by histological methods. In these several publications the whole cortex cerebri of man, and in many orders of mammals, has been mapped out into various histologically different regions; and in some instances proof of the functional significance of these has also been adduced. Further, the mode of evolution and functional significance of the different cell-laminæ of the cortex cerebri have been discussed from both the ontogenetic and the phylogenetic aspects.

As I purpose in these lectures to deal solely with the human cerebrum, it is unnecessary for me to refer, except as occasion serves, to such investigations as concern the cortex of the lower mammals. Amongst the publications which bear on cortical localization in man, those of two authors stand out prominently — namely, the "Histological Studies" of Campbell [10] and the series of monographs published since the year 1902 by Brodmann [8]. These authors have independently and elaborately mapped out into histologically different areas the whole human cortex cerebri as well as the cortex cerebri of certain orders of mammals.

The human maps of these authors, whilst differing considerably in detail, agree with one another much more than either of them resembles the maps of Flechsig. I have already indicated one reason why the map of Flechsig cannot be applied directly to the adult cerebrum. It will also be evident to you that, owing to the low development in the fœtus of the later evolved spheres of association, the projection areas must of necessity differ considerably in their relative size and distribution in the fœtus and the adult. Further, without going so far as Elliot Smith [20], who from the point of view of causation closely correlates fissuration and histological differentiation, although these differ very considerably in the adult cerebrum, I certainly regard histological differentiation as one of the causes of fissuration, others being arterial supply, and probably also certain mechanical conditions of growth. It is hence not surprising that the projection areas of Flechsig, taking for granted their correctness in the fœtus, do not bear the same relationship to the main cerebral fissures as do these areas in the adult cerebrum.

Compare the maps of Flechsig (figs. 1 and 2) with the maps of Campbell and of Brodmann. It will be noticed that the visuo-sensory area is much larger than in the adult, as is also the bodily sensibility projection centre, which, in the adult, lies entirely behind

the fissure of Rolando. Flechsig, however, I may remark, expressly states that the majority of the projection fibres pass behind the central fissure. At the period when the experimentally-obtained Rolandic

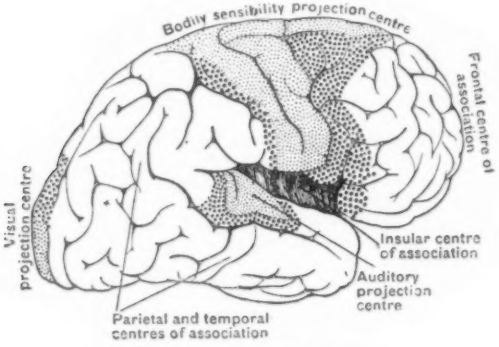
Bodily sensibility projection centre
Frontal centre of association
Visual projection centre
Insular centre of association
Auditory projection centre
Parietal and temporal centres of association

FIG. 1 (AFTER FLECHSIG).

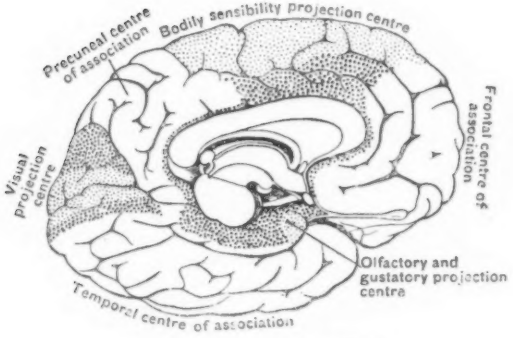
Precuneal centre of association
Bodily sensibility projection centre
Frontal centre of association
Visual projection centre
Olfactory and gustatory projection centre
Temporal centre of association

FIG. 2 (AFTER FLECHSIG).

In these diagrams the "centres of projection" and "centres of association" are mapped out according to Flechsig. The small dots are placed in the chief focus of each centre of projection. Around these chief foci are the regions to which a smaller number of fibres of projection pass; these are indicated by larger dots. These figures, which represent the different cortical spheres indicated by Flechsig as the result of his embryological studies, should be compared with figs. 3 to 6, and 7 and 8, which illustrate the various areas into which the adult cerebral cortex has been subdivided by Campbell and Brodmann respectively.

area was considered to be both pre- and post-Rolandic, and to be sensori-motor in function, its supposed distribution closely resembled the fœtal bodily sensibility area of Flechsig, and the two were regarded

as identical. Now, however, the "motor" and "sensory" areas are regarded as separate and as lying on either side of the furrow of Rolando. It is, by the way, necessary to remark in this connexion, lest I should

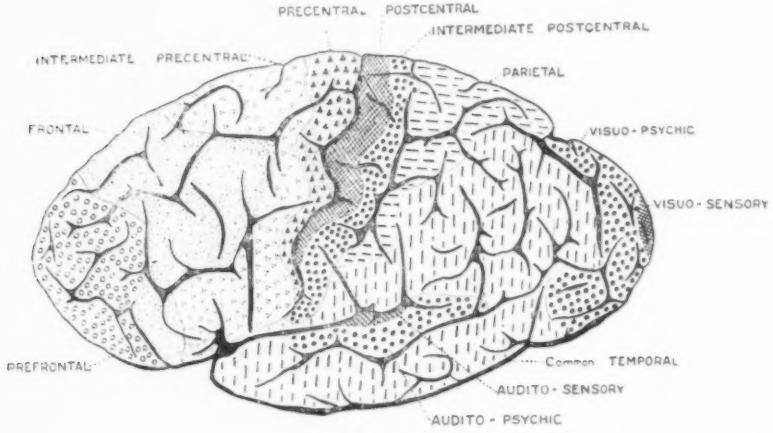

FIG. 3 (Campbell, 1904)

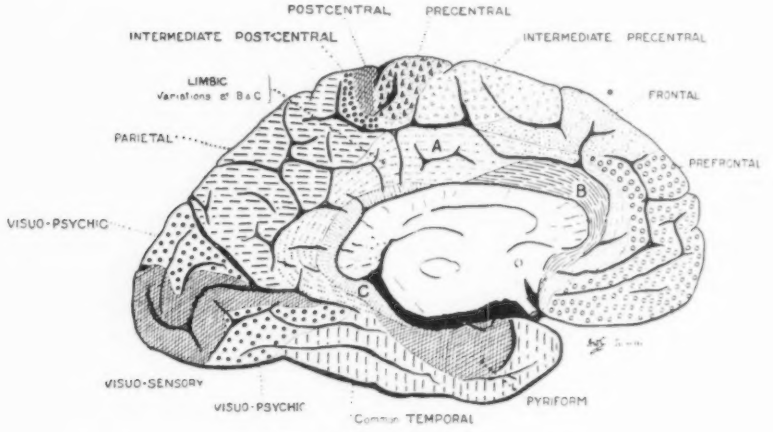

FIG. 4 (Campbell, 1904).

appear to disregard a recent article by Horsley [15], that I intend to refer to this when dealing later with the structure and functions of the psychomotor area.

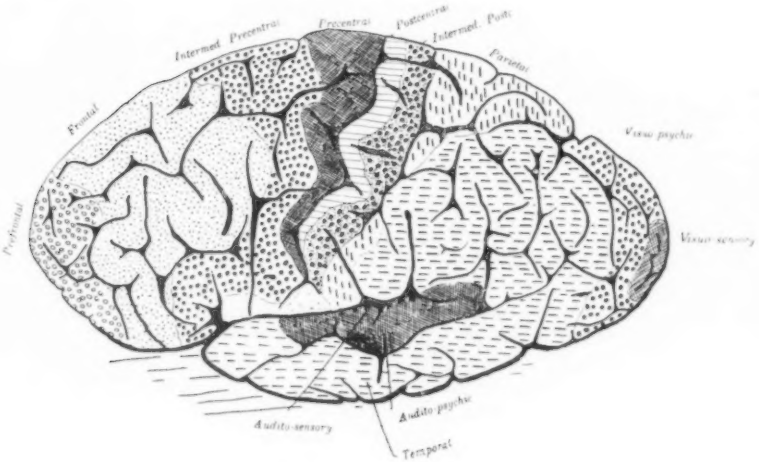

FIG. 5 (Campbell, 1905).

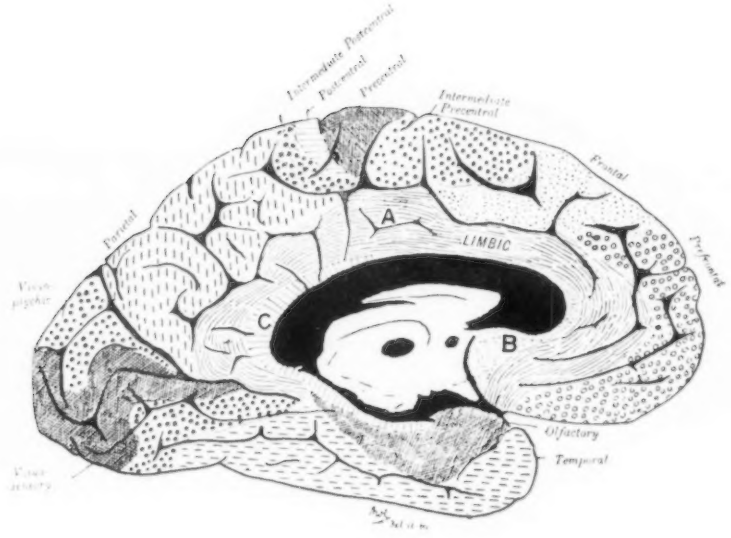

FIG. 6 (Campbell, 1905).

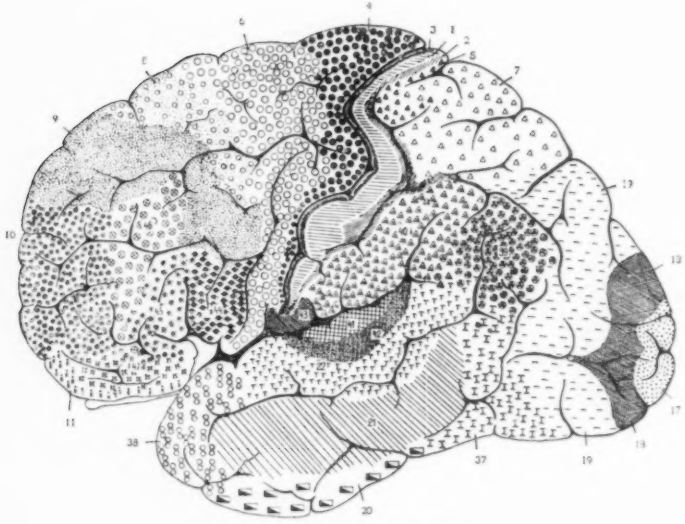

FIG. 7 (Brodmann. 1902-1907).

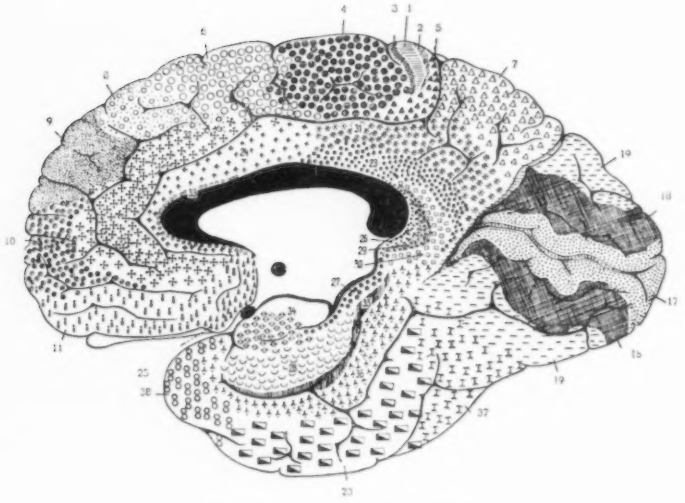

FIG. 8 (Brodmann. 1902-1907).

On figs. 3 to 8 I have arranged for comparison two sets of maps by Campbell, published in the years 1904 and 1905, and the maps of Brodmann.

In view of the great difficulties involved in cutting up, blocking, sectioning, orientating and reproducing in diagram form the cortex of entire human hemispheres, considerable differences might well be expected in maps prepared by two totally independent investigators. It is, however, difficult to understand the well-marked differences which exist in the case of the two pairs of diagrams of Campbell, one of which is contained in a preliminary communication, and the other, very shortly afterwards, in his monograph, since the fissuration of the two is identical. In the case of the prefrontal, the frontal, the parietal, and the visuo-psychic regions, the differences in distribution are very considerable, in view of the fact that, in the case of a particular brain, either the lines of demarcation should be very exact, say, within a millimetre in different copies of the same brain, or they should be left indefinite.

On the face of it, the maps of Campbell appear to be the more diagrammatic and the less accurate of the two sets; and this impression has been confirmed from my personal acquaintance with many regions of the cortex, particularly the frontal lobe and the visual areas. I would also refer to a recent paper by Gordon Holmes [13], on the histology of the post-central gyrus, in which the findings of Brodmann are confirmed.

I am, nevertheless, of the opinion, without disputing in any way the entire accuracy of these particular maps of Brodmann, that the exact differentiation of the greater portion of the grey mantle into such relatively precise areas as are the Betz-cell area and the visuo-sensory area will be attended with great difficulty owing to the probability that considerable differences exist in the case of different individuals, and especially so in the case of the poorly developed brains which are often met with in asylum practice. As an illustration of my meaning I have put together a diagram of six occipital regions [2] in which, many years ago, I precisely mapped out and obtained proof of the functional significance of the visuo-sensory area (fig. 9).

It will be noticed that both the shape and the apparent extent of this area differ considerably in the several cases, even when difference of age or the existence, in some, of long-standing blindness is allowed for.

Case 1 is a normal male aged 55 years.

Case 2, a female aged 17 years, is an example of chronic insanity with epilepsy.

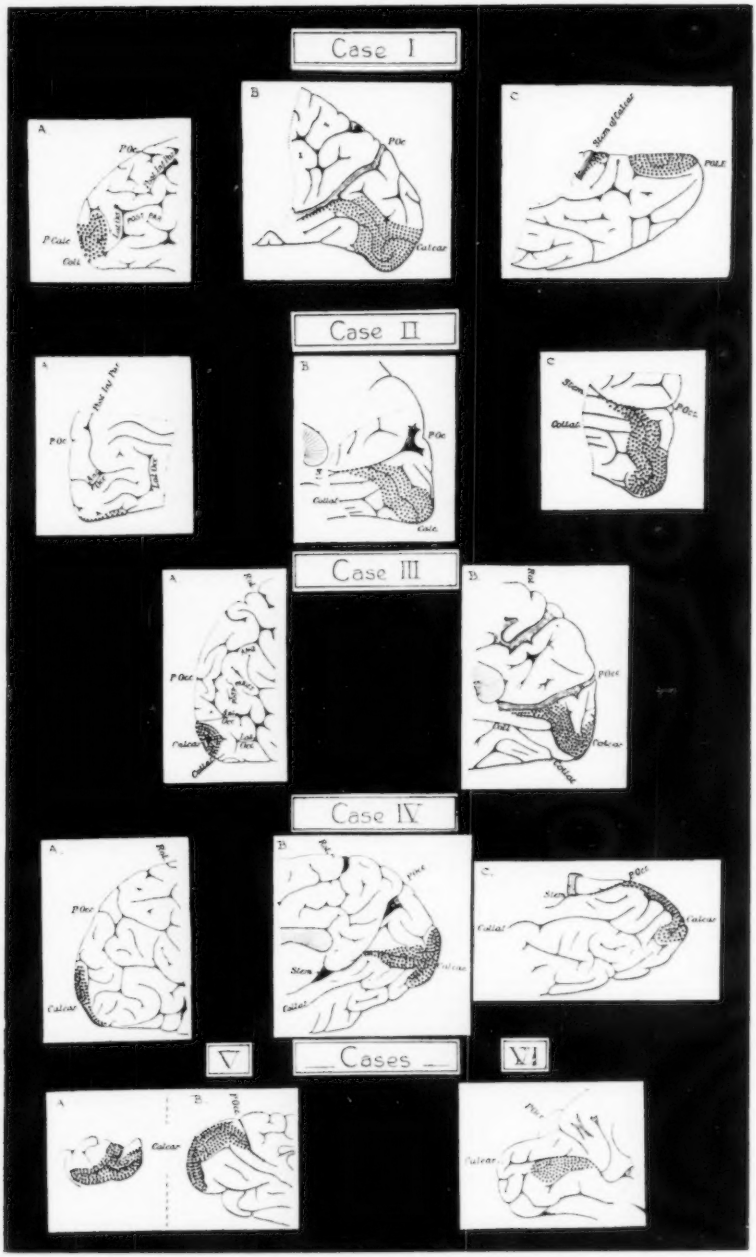

FIG. 9.

The figure illustrates variations in the distribution and the extent of the visuo-sensory area in different brains. Case 1.—Normal male, aged 55. Case 2.—Female, aged 17, chronic insanity with epilepsy. Case 3.—Female, aged 27, chronic insanity with blindness from infancy. Case 4.—Male, aged 30, chronic insanity with long-standing blindness. Case 5.—Normal infant, aged 3 months. Case 6.—Anophthalmos, aged 1 month. A = outer surface of hemisphere; B = inner surface; C = under surface.

Case 3, a female aged 27 years, is an example of chronic insanity with blindness from infancy.

Case 4, a male aged 30 years, is an example of chronic insanity with long-standing blindness.

Case 5 is a normal infant, male, aged 3 months, and

Case 6 is an example of anophthalmos, aged 1 month.

If such individual differences exist in a projection area of early evolution and stable organization, it is, to say the least, likely that still greater individual differences exist in the later evolved and later specialized regions of association.

As another illustration, this time of probable individual variation only, I will refer in a few words to the recent researches of Marie [18] concerning aphasia and the functions of the area of Broca. It may be accepted, as I have elsewhere [3] remarked, that the thesis of this author, with regard to the intellectual impairment exhibited by all aphasics, is true, at any rate if such cases be studied by methods familiar to the alienist. It is not, however, probable that motor aphasia is invariably the result of anarthria + sensory aphasia, although, on the other hand, it is doubtless true that anarthria + sensory aphasia necessarily give rise to the symptomatology of classical motor aphasia. It is certain that in the case of many persons Broca's speech centre is rightly disrated by Marie, whereas it is extremely probable that in others Broca's area is part of the educated psychomotor area, in which case its permanent loss would result in temporary "motor aphasia" with temporary interference with voluntary thought. Such variability with regard to the individual distribution of the special part of the psychomotor area which subserves the evolution of speech is, in my opinion, the only possible explanation of the widely divergent views which are held by equally competent observers.

Before concluding my reference to the histological differentiation of the cortex, I wish to mention quite briefly another question of importance. I have indicated the probability, if not certainty, that individual variations occur in the actual extent occupied by the several histologically differentiated areas which have been described. Whilst histological differentiation probably indicates the limits of possible educability, it does not, however, necessitate the existence of functional activity.

A very obvious illustration of this truth may be seen in the motor exhibitions evolved by the psychomotor area, which constitute the sole objective indications of cerebral activity. Whether we consider the infinite variety of skilled movements, the numerous highly complex

written and spoken languages, or the wonderful gamut of expression and gesture of which the intelligent human subject is capable, we see in each case gross individual differences in educability. Histological differentiation probably supplies the key with regard to individual potentialities, but it is doubtful whether any single individual of the race has ever even approached the limits of his potential education.

I will trouble you with but one further illustration—namely, the remarkable manner in which such serious disabilities as congenital or early deprivation of the senses of hearing or sight may be compensated by education [14].

A person suffering from congenital or early loss of hearing is necessarily dumb; and, unless he live in association with other individuals suffering from the same disability, or be educated by special means, his mental functions differ little from those of the anthropoid apes. In such persons, under either of these conditions, the auditory disability is compensated for by shrewdness of vision, and the speech disability by the evolution of descriptive mimicry to a high standard. The deaf and dumb think by mimicry just as voluntary thought in normal persons occurs by the preliminary activity of the articulatory part of the psychomotor area, which is important evidence, if such be needed, in favour of the truth of the latter thesis. A normal individual may "think to himself" by means of invisible laryngeal and respiratory movements. A deaf-and-dumb person does not possess the same involuntary ability to hide the results of psychomotor activity during voluntary thought. Further, if such be taught lip-language, they readily learn to communicate with normal persons inexperienced in the special mimicry of the deaf and dumb.

On the other hand, the congenitally or early blind acquire language just as do ordinary non-reading and non-writing individuals, and, in the absence of special education, exhibit little or no defect of the mental functions. In such persons, however, loss of sight is usually compensated by marked hyperactivity of the sense of touch; and by means of special type the blind are able to acquire education which is often little, if at all, inferior to that of many normal individuals.

After these general remarks, I pass to the subject I purpose laying before you—namely, the evidence which I have obtained from the clinico-pathological study of mental disease, with regard to the functional significance of certain special cortical areas.

I have hitherto confined my attention to four of the numerous regions into which the cerebral cortex is divisible—the visuo-sensory area, which is the best example of the sensory projection spheres; the visuo-psychic zone, which is one of the regions of special cerebral association; and the prefrontal (higher psychic) and precentral (psychomotor) regions.

As necessary preliminaries, I shall now describe in detail the method which I have employed, and also the manner in which the cortex cerebri undergoes evolution during fœtal life and infancy.

Chapter II.

Method of Investigation.

The method which I am about to describe, and which I have employed for many years, is that of micrometric measurement of the primary cell- and fibre-laminæ of the cortex. Neither in detail nor in results is it in any way comparable with the macro- and micrometric mensuration of grey matter which has been performed by several workers for many years, and it is therefore not necessary for me to refer further to this.

For reasons which I shall indicate later, I am accustomed to subdivide the cortex, for the purposes of measurement, into the five primary laminæ from which it has been evolved—namely, (1) the *outer fibre-lamina* or superficial layer; (2) the *outer cell-lamina* or pyramidal layer; (3) the *middle cell-lamina* or granule-layer; (4) the *inner fibre-lamina* or inner line of Baillarger, which in certain regions contains such bodies as the Betz cells and the solitary cells of Meynert; and (5) the *inner cell-lamina* or polymorphic layer. These five laminæ may more or less readily be identified in all parts of the neopallium, though they differ in their degree of development in different cortical areas. For example, in the psychomotor area, the third lamina is of minimal depth and can only be detected by careful examination. On the other hand, in the visuo-sensory area, the third lamina is of great depth, the granule-layer being duplicated by the interposition in its midst of the fibre-layer of Gennari, in which terminate the fibres of the optic radiations.

For the micrometric examination of the cortex it is, however, not sufficient merely to determine the laminæ which it is proposed to measure. Granted that accurately vertical sections are obtained, it is further necessary to define the exact regions of the convolutions which are capable of measurement. In theory the flat external surface of the

convolutions is the ideal region, and in certain fœtal brains it is the only one which is available. In practice, however, its sole employment is impossible, if only for the sufficient reasons that a trustworthy number of situations is rarely available, and that its degree of development varies greatly, being very different over broad and narrow convolutions. I consequently employ four regions of the convolutions, and from these prepare a general average measurement. These regions are the *flat surfaces* or external parts between fissure lips, the *apices* or fissure lips, the *bottoms* of fissures, and the *sides* of fissures at some point between the apices or fissure lips and the bottoms of the fissures.

These regions are shown in the diagram (fig. 10).

It is perhaps hardly necessary to remark that in any given section, though it be cut ever so truly, many obliquities exist, and only a certain number of regions can be selected. In fact, it is by no means easy to obtain the necessary number of regions for measurement, and it sometimes happens that cases of promise have to be rejected, even after all the sections have been cut and stained.

The four well-defined regions to which I have referred are alone capable of accurate micrometric measurement, and for reasons which I shall now give, it is possible, after a sufficient number of measurements from these have been averaged, to obtain a trustworthy general average measurement from the four, which can be employed for the comparison of case with case.

Taking the four regions in turn, in the case of the *flat surface*, the fourth and fifth laminæ, and usually the third, are above the general average measurements, in some broad flat surfaces slightly, and in some narrow ones markedly. In the case of the *sides* of fissures, laminæ four and five are, as a rule, below the general average measurements, and considerable variation as regards total depth occurs in this region. As, however, many side measurements are, as a rule, available, it is relatively easy to obtain a trustworthy average. Flat surfaces and sides thus, in a measure, when taken together neutralize the defects inherent to each. In the case of the *apices*, the first two laminæ are, as a rule, slightly below the general average measurements, whereas lamina three is usually slightly above, lamina four is markedly above, and lamina five is considerably above the general average measurements. Lastly, in the case of the *bottoms* of fissures, lamina one is considerably above the general average measurement, and lamina two is slightly below, lamina three is moderately below, lamina four is very

REGIONS OF CORTEX CHOSEN FOR MICROMETRIC MEASUREMENT

'A' · APEX , 'B' · BOTTOM . 'F' · FLAT . 'S' · SIDE

MEASUREMENTS OF VISUO-PSYCHIC CORTEX OF NORMAL ADULT

REGIONS OF CONVOLUTIONS	I	II	III	IV	V
SIDE AVERAGE OF 36	285	609	200	177	243
APEX AVERAGE OF 35	252	665	218	189	410
BOTTOM AVERAGE OF 12	149	737	165	067	166
FLAT AVERAGE OF 19	295	948	221	282	354
GENERAL AVERAGE IN MM (26)	274	864	200	229	293

DITTO OF INFANT, AGED 3 MONTHS

REGIONS OF CONVOLUTIONS	I	II	III	IV	V
SIDE AVERAGE OF 18	229	721	162	136	214
APEX AVERAGE OF 16	178	700	206	568	297
BOTTOM AVERAGE OF 6	327	896	168	082	150
FLAT AVERAGE OF 3	236	786	221	251	236
GENERAL AVERAGE IN MM (34)	243	876	191	212	274

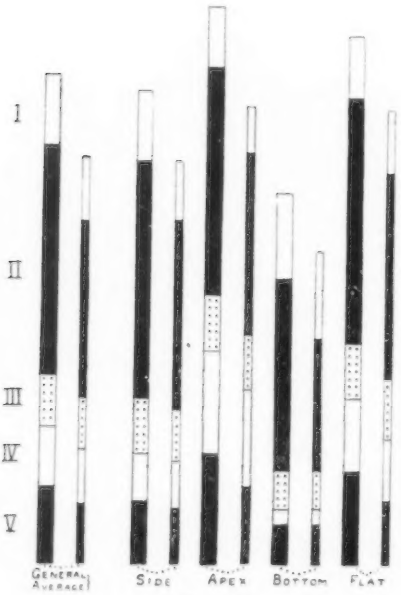

FIG. 10.

The figure illustrates the method of micrometric measurement. In the upper portion of the figure are shown the four regions of the convolutions, which alone are capable of satisfactory measurement. In the middle part the results of the micrometric measurement of the visuo-psychic cortex of a normal adult and of an infant aged 3 months are given. In the lower portion the different cortical laminæ are shown graphically. These from above downwards are (I) the outer fibre- or superficial lamina; (II) the outer cell- or pyramidal lamina; (III) the middle cell- or granule-lamina; (IV) the inner fibre-lamina or inner line of Baillarger; and (V) the inner cell- or polymorphic lamina. On the left-hand side are shown the general average measurements obtained from a normal adult and an infant aged three months respectively; and on the right-hand side the average "side," "apex," "bottom," and "flat" measurements from which these general average measurements are produced.

much below, and lamina five is greatly below the general average measurements. Apices and bottoms, when taken together, thus to a great extent neutralize the defects inherent to each, and it is probable that, when a general average measurement is made from all four regions, a result is obtained which differs little from the measurements that would be obtained were the whole cortex a smooth, flat surface without fissures. Such a general average measurement as I have described, I believe to be entirely satisfactory for the comparison of different cases with one another.

In the diagram are illustrated the general average measurements of a normal case, and of an infant aged three months, and also the average measurements of the sides, apices, bottoms, and flat surfaces of each of these cases.

I would remark here that these differences in the depths of the several laminæ in the four regions are susceptible of a mechanical or structural explanation, which serves as a further justification for the employment of the four for the production of a general average measurement, since different cases, and also different cortical areas, vary in the degree to which such variations occur.

As has been remarked, at the apices the outer two laminæ are decreased, the third is slightly increased, the fourth is more than doubled, and the fifth is much increased. In the case of the flat surfaces a similar increase occurs in the lower three laminæ. At the bottom of the fissures, on the other hand, whilst the first lamina is increased, all the others, especially the fourth, are decreased; and in the case of the sides the fourth and fifth laminæ are somewhat decreased.

It is probable that these variations are due to the folding of the grey matter, for at the apices the convex outer surface would from this cause be relatively more extended and the laminæ consequently be thinned, whilst, on the contrary, the inner layers would be much crowded and increased in depth, this condition being intensified by the radiating manner in which the cortico-petal and the cortico-fugal fibres would necessarily have to pass in order to reach the convex surface. Owing to this radiation of fibres, some slight thickening should also occur in the third lamina. On the other hand, at the bottom of the fissure the first lamina would necessarily be thickened, owing to the large mass of fibres it would have to contain in spite of the relatively abrupt bend; and for the same reason the deeper layers would be thinned, partly because they occupy a relatively large convex area compared with the abrupt bend of the outer laminæ, and partly because of the relatively

smaller number of cortico-petal and cortico-fugal fibres which would require to pass through their convex extension of surface. If to this be added that the surface convexity is necessarily larger in extent than the sharp bend at the bottom of the sulci, owing to the fact that fibres have to pass to and from all the surface parts of the cortex along the centre of the gyrus, and that the larger the external portion becomes the more acute is the bend at the bottom of the fissure, the mechanical or structural explanation of local variations in depth appears to be an entirely satisfactory one.

In individual cases gyri vary greatly in size, and the bends at the bottoms of fissures vary greatly in acuteness. Hence, regional variations differ in degree according to the particular case.

Lastly, from the aspect of different cortical areas, in the case, for example, of the visuo-sensory area many more fibres pass to the cortex than in the case of the visuo-psychic region, and in conformity with this fact the thinning of the layers at the bottoms of the fissures of the former (though actually less in degree) is relatively much more definite than is the alteration in depth of the various laminæ of the apices and flat surfaces: in other words, the gyri are more rounded, the layers are less moulded by position, and at the same time the bends at the bottoms of the fissures are relatively more abrupt.

For these various reasons I think it must be ceded that a general average measurement obtained from average measurements of the four regions I have defined is entirely trustworthy for the comparison of cases with another.

In the case of this and the following lecture, the measurements which I purpose to present in diagrammatic form have all been prepared in this manner. As the conclusions which I draw from them depend entirely on the accuracy of the method which I have adopted, I have thought it necessary to deal with this method in considerable detail.

A word is here necessary with regard to the method of preparation of the tissue employed. All the hemispheres have been hardened in 5-per-cent. commercial formalin; and the sections, though prepared and stained by different methods, have all been mounted in canada balsam. I was at one time of the opinion that different methods of sectioning and different methods of staining might result in quite different micrometric results; and my various series of cases were kept distinct from one another—e.g., cases cut by freezing or in paraffin, or stained by modified Nissl or ammonia-iron-alum-hæmatoxylin, &c. Comparison of the various micrometric

results obtained from the same or different cases, cut and stained by the same or different methods, has, however, satisfied me that the question of method is of no importance, granted that the tissues are hardened and mounted in the same manner. The original hardening reagent appears to determine once for all the bulk of the hardened tissue, and any modifications which occur later, in consequence of the reasonable employment of reagents of different specific gravities, become readjusted when the tissue has been finally mounted in canada balsam.

The micrometric measurements are made by means of a Zeiss A objective and a No. 2 eyepiece with a tube of 160 mm. They are then reduced to micro-millimetres by the constant (14·73) of this particular combination. As the constant varies somewhat in the case of different lenses of the same manufacture, I have throughout my work rendered the results strictly comparative by the employment of a microscope and lenses for the special purpose of micrometric measurement.

The special regions of the human cortex cerebri which I have hitherto dealt with by this method are the visuo-sensory, the visuo-psychic, and the prefrontal, as the most satisfactory examples available of projection, hall-marked or special associational, and higher associational cortex. The reasons for this selection will appear later.

I have, in all, measured fifty-four regions in thirty-eight hemispheres, which were obtained from thirty-seven cases of various types, including three fœtuses, two stillborns, three infants, four normal cases, and twenty-five examples of various types of mental disease, grading from the idiot with very deficient cerebral evolution, through imbeciles, recent, chronic and recurrent non-demented lunatics, and partially demented lunatics, to the gross dement with great cerebral dissolution.

Of the fifty-four regions measured, fifteen are visuo-sensory, fifteen are visuo-psychic, and twenty-four are prefrontal.

The visuo-sensory and visuo-psychic results are from the same cases, and in theory it would appear desirable that all the regions should have been examined in every case. In practice, however, this has been impossible, owing to the laborious nature of the work and the length of time it has been in progress. It has also been found to be unnecessary, on the one hand because the differences in measurement are well marked and definite, and on the other because the results of prefrontal measurement are of a different type from those obtained from the visuo-sensory and visuo-psychic regions. I may add that it has, in consequence, been possible up to the present to measure a much larger series of cases than would otherwise have been available. I have, however,

specially selected a suitable, well-marked case, and measured all the three regions, in order to obviate such a possible criticism, and to prove the points to which I have just referred.

Chapter III.

The Lamination of the Normal Cortex and its Mode of Evolution.

I purpose demonstrating in the second lecture that the essential physical basis of mental disease consists, on the one hand in an imperfect development of the cell-laminæ of the cortex which is of the nature of a true sub-evolution, and on the other in degrees of decrease of the cell-laminæ which are of the nature of a true involution or dissolution, since such decrease in depth takes place in the converse order to that in which the cell-laminæ are developed during the process of normal growth.

Fig. 11.

Outer surface of the right hemisphere of a male fœtus, aged a little over four months. Weight, after hardening in formalin, 32 grm. The fissure of Sylvius and a depression which occupies the site of the future fissure of Rolando are present, as also are numerous vascular grooves. Figs. 11, 13, 15, and 17 are of the same relative size.

As one of the necessary preliminaries to this demonstration, it is therefore desirable to describe in some detail the normal mode of evolution of the lamination of the cortex. For this purpose I shall employ the prefrontal region, since this is the portion of the cerebrum which is the last to be normally evolved, and also the area in which are present in maximum intensity those indications of sub-evolution and involution which occur in cases of mental disease.

The plates which I shall now describe are intended to show from the general point of view the manner in which the lamination of the cortex becomes evolved. All the microphotographs of this series are of exactly the same magnification.

The first photograph represents the right hemisphere of a human fœtus of about four months (fig. 11). The fissure of Sylvius and a

depression which occupies the site of the future fissure of Rolando are present, as also are numerous vascular grooves.

In the following microphotograph (fig. 12) is shown a section of the prefrontal cortex. This will be seen to consist of a layer of

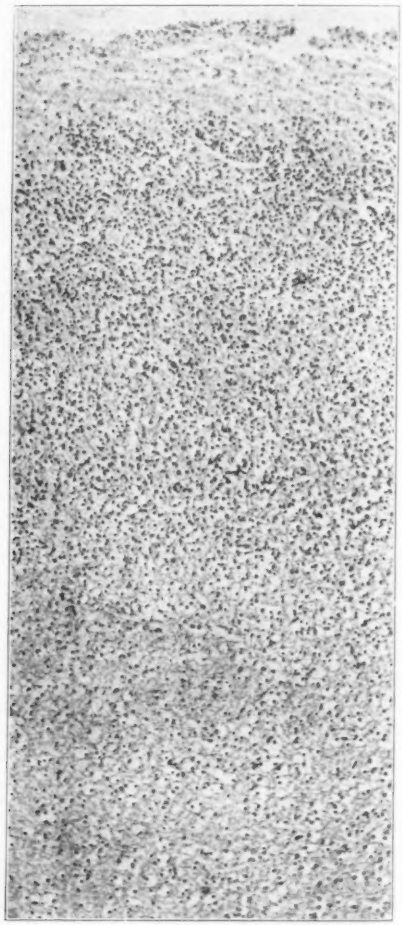

FIG. 12.

One hundred and nine diameters. The prefrontal cortex of the hemisphere shown in fig. 11. It consists of a layer of undifferentiated neuroblasts covered by a superficial layer of neuroglia into which irregular masses of neuroblasts project.

undifferentiated neuroblasts covered by a superficial layer of neuroglia, into which irregular masses of neuroblasts project. The neuroblasts are most closely packed towards the surface, and, at about the level of the lower trisection, indications exist of commencing differentiation of the nerve cells. The cortex has not begun to laminate, and its total depth is less than one-half of that of the normal adult.

In the next photograph (fig. 13) is shown the left hemisphere of a fœtus of about six months. The brain is somewhat larger and firmer, and the main fissures are defined or appearing. The numerous vascular groves seen in the previous hemisphere have largely or entirely disappeared, and the prefrontal region of the cortex consists simply of a flat external surface.

FIG. 13.

Outer surface of the left hemisphere of a fœtus, aged a little over six months. Weight, after hardening in formalin, 55 grm. The main fissures are defined or appearing, and the brain is larger and firmer than that shown in fig. 11.

The prefrontal cortex, as is seen in the microphotograph (fig. 14), shows little increase in depth, but definite signs of the commencement of the process of lamination. The inner cell-lamina or polymorphic layer is being separated from the rest by the development of the inner fibre-lamina or inner line of Baillarger. The middle cell-lamina or granule-layer is visible, owing to the shape and mode of aggregation of its constituent cells, and the outer cell-lamina or pyramidal layer can also be made out, and exhibits a partially columnar arrangement of its constituent cells in its lower two-thirds, and a massing together of the cells in its upper third. It will be at once evident to anyone familiar with the appearance of the adult cortex that development is taking place from within outwards, and that the superficial laminæ, especially the outer cell or pyramidal, are as yet of very deficient depth, the last being only about one-fourth of the adult normal.

It will be noted, on comparing the fourth and sixth months' fœtuses, that the development of lamination is coincident with greater firmness

of the brain and disappearance of the numerous vascular grooves, rather than with any notable increase in the complexity or size of the hemispheres. Microscopically, however, an important advance has occurred—namely, the commencement of the process of lamination and a cleavage of the neuroblasts into an upper and a lower portion. In view

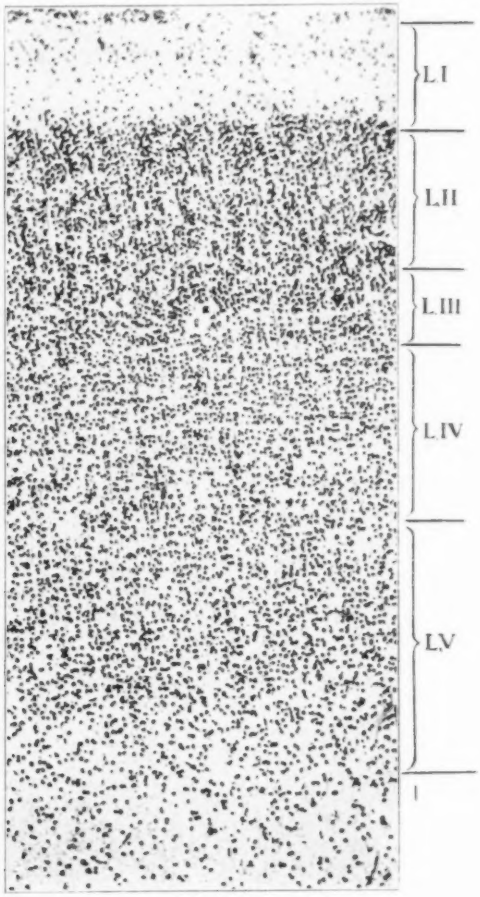

FIG. 14.

One hundred and nine diameters. The prefrontal cortex of the hemisphere shown in fig. 13. The process of lamination has commenced. L.I, the outer fibre-lamina. L.II, the outer cell- or pyramidal lamina. L.III, the middle cell- or granule-lamina. L.IV, the inner fibre-lamina. L.V, the inner cell- or polymorphic lamina.

of the evidence I shall produce with regard to the functions of the inner cell-lamina, I would remark that this early cleavage of the partially differentiated neuroblasts of the cortex into an upper and a lower portion is an occurrence of the greatest significance.

The next photograph (fig. 15) is of the right hemisphere of a fœtus of seven to eight months. The fissuration is completed, with the exception of the less important sub-sulci, and the brain has a general resemblance to that of the adult.

As is shown in the accompanying microphotograph (fig. 16), marked progress has taken place with regard to the development of the cortex and the differentiation of the nerve cells. The inner cell-lamina is clearly marked off by the inner fibre-lamina from the middle cell-lamina, and the outer cell-lamina or pyramidal layer shows a notable increase both in the depth of its lower part and in the degree of differentiation of the constituent cells of this. The upper portion of

FIG. 15.

Outer surface of the right hemisphere of a fœtus, aged 7 to 8 months. Weight, after hardening in sublimate and formalin, 56 grm. The fissuration is completed, with the exception of the less important sub-sulci.

this lamina is still in a poorly differentiated condition, and the aggregation of its embryonic constituent cells is by contrast more visible than is the case in the fœtus of six months.

In the next photograph (fig. 17) is shown the unstripped right hemisphere of a stillborn male infant. The resemblance to the adult appearance of the brain is now well marked.

In the microphotograph (fig. 18) it will be seen that the cortex now exhibits a general resemblance to that of the adult. The nerve cells have largely taken their permanent form, and, being less embryonic and smaller, appear less crowded. A further important factor in causing less aggregation of cells is the increased superficial area of cortex, and the consequent smaller number of cells in a section of

the same thickness. The outer cell-lamina or pyramidal layer is, however, still little more than one-half of the adult normal depth.

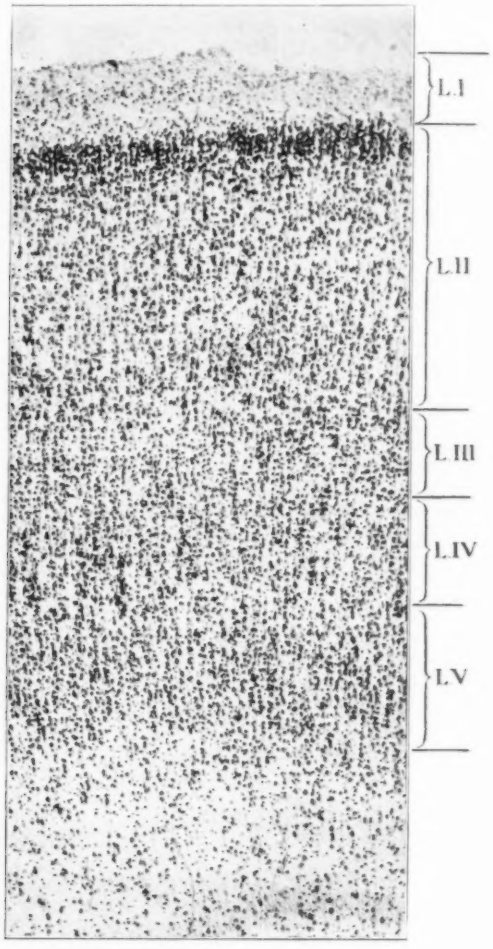

FIG. 16.

One hundred and nine diameters. The prefrontal cortex of the hemisphere shown in fig. 15. L.I to L.V as in fig. 14. L.II, the outer cell- or pyramidal lamina, though the latest to develop, has already become the deepest layer of the cortex. In the upper portion of this lamina the aggregation of its embryonic constituent cells is by contrast more visible than is the case in the fœtus of six months.

and exhibits a very obvious aggregation of embryonic cells in its upper part.

In contrast to the preceding microphotographs, the plate on p. 51 (fig. 19) illustrates the depth and general appearance of the adult normal cortex. The magnification is five-sevenths of that of the preceding microphotographs.

It was originally my intention to follow the further development of the cortex in children of different ages, but I found that such notable individual differences in the degree of the development of the cortex occurred as precluded the possibility of obtaining definite results. This truth is the anatomical counterpart of the known great individual differences in degree of mental development which exist in infants and young children.

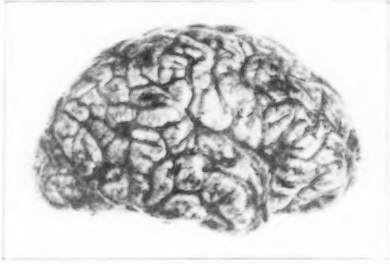

FIG. 17.

Outer surface of the unstripped right hemisphere of a male full-term stillborn child. Weight, after hardening in formalin, 194 grm. The fissure of Sylvius remains somewhat open, and its posterior limb is very oblique. The prefrontal region is small.

In the diagram on p. 52 (fig. 20) are shown, in percentages of the normal, the general average measurements which I have obtained from the prefrontal cortex of a number of cases. They clearly indicate the point to which I have just referred. The second case, though it falls well into series with the remainder, exhibits certain differences in the depth of the fourth and fifth laminæ which are due probably to the fact that all the measurements are from the flat external surface, owing to the absence of fissures. The fourth and fifth cases exhibit the individual differences in degree of development which I found to occur in two stillborn infants; and the case in the sixth column, that of a marasmatic infant of retarded general development, is also interesting in that the outer cell-lamina is of less depth than that of the second stillborn, whilst all the other laminæ are of almost

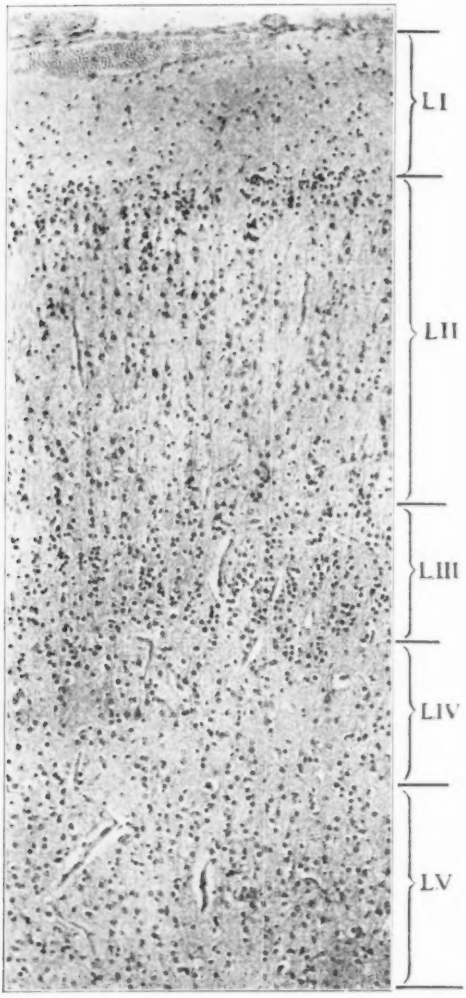

FIG. 18.

One hundred and nine diameters. The prefrontal cortex of the hemi-sphere shown in fig. 17. L.I to L.V as in preceding microphotographs. The cortex much more resembles that of the adult. L.II, the outer cell- or pyramidal lamina is, however, still little more than one-half of the adult normal depth, and exhibits a very obvious aggregation of embryonic cells in its upper part.

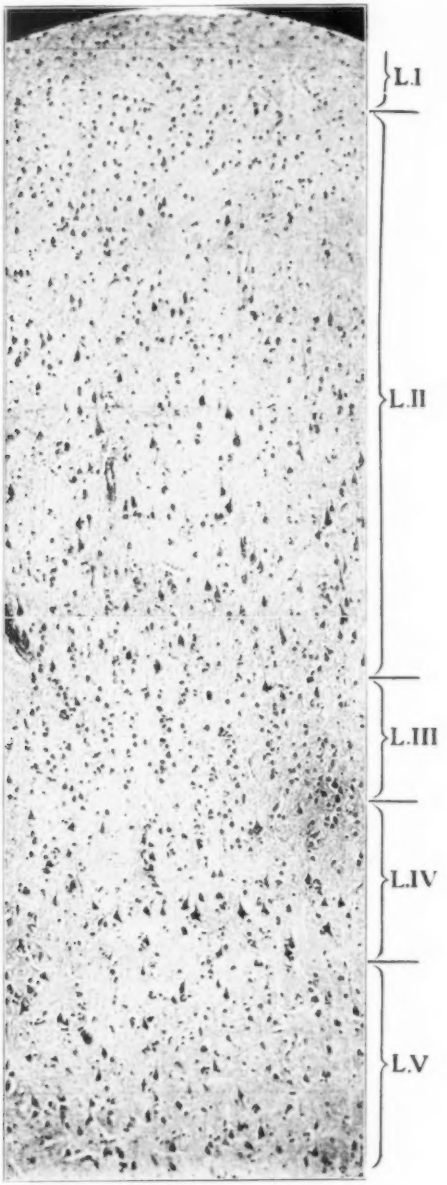

FIG. 19.

Seventy-six diameters. The prefrontal cortex of the normal adult. The magnification is five-sevenths of that of the preceding microphotographs. L.I to L.V as in previous figures. It should be noted that the depth of L.II is greater than the conjoined depths of L.III to L.V.

exactly the same depth as are those in the latter. Further, the diagram shows quite definitely that the laminæ are evolved from within outwards, and that the inner cell-lamina approaches the adult

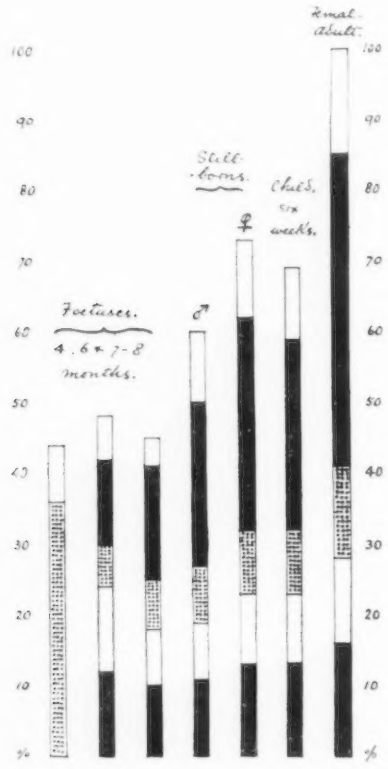

FIG. 20.

The figure shows, in percentages of the normal, the general average measurements of the prefrontal cortex of a series of fœtuses and infants. The actual measurements of these cases, together with other details concerning them, are summarized in Appendix A. The laminæ from above down are as in preceding figures. The illustration indicates that the cortex evolves from within outwards, the inner cell-lamina being the first to appear and rapidly attaining almost to the adult depth, and the outer cell-lamina the last, this lamina at birth being still only about one-half of the adult normal depth.

normal depth at birth, at which date the middle cell-lamina is about three-fourths, and the outer cell-lamina still little more than one half of the adult normal depth.

The same order of evolution of cortical lamination applies, judging from sample observations I have made, to the whole neopallium, though differences exist, both with regard to the degree of development of the different laminæ and to the date at which it occurs.

The outer cell-lamina or pyramidal layer, for example, in the visuo-sensory area attains in the adult to but five-ninths of the adult normal average depth, and elsewhere, as far as my observations extend, is of more constant depth, with measurable individual variations. The middle cell-lamina or granule-layer, in the visuo-sensory area, is hypertrophied and duplicated by the interposition of the fibre-layer of Gennari; its total depth, including this, being about three-and-a-half times its depth generally. On the other hand, in the psychomotor area, the granule-layer reaches a minimum depth, and is with difficulty discernible. The inner cell-lamina is of very constant depth. It is somewhat shallow in the visuo-sensory area, though proportionately less shallow than is the outer cell-lamina in this region.

With regard to the date at which evolution of the cortical laminæ occurs, I have at present merely sufficient evidence to show that it takes place earlier in the visuo-sensory area (projection sphere) than in the visuo-psychic (zone of special association), and earlier in the latter than in the prefrontal region (zone of higher association).

This evidence is shown in the following diagram (fig. 21), in which are collected a series of observations on the cortex of certain fœtuses, infants, and adults. The following are the chief points illustrated in the figure. In the visuo-sensory area of the infants of one and three months, the whole of the cell-laminæ have attained to almost the normal adult depth, and the outer cell-lamina is rather better evolved in the former than in the latter, in spite of the existence of congenital blindness in that case. On the other hand, in the visuo-psychic zone none of the laminæ are so far evolved, and the outer cell-lamina of the infant of one month is much shallower than that of the infant of three months. The visuo-sensory cortex is thus obviously evolved earlier than is the visuo-psychic. A further interesting point shown in the diagram is the low evolution of the middle cell-lamina, or receptive layer, of the cortex of the congenitally blind infant of one month, and the almost adult development of this in the infant of three months. The same detail is visible in the case of the visuo-psychic region, and this alone is sufficient to hallmark the visuo-psychic region as a zone of special visual association, especially when it is noted that this lamina is in the infant of three months of practically the adult depth, whereas

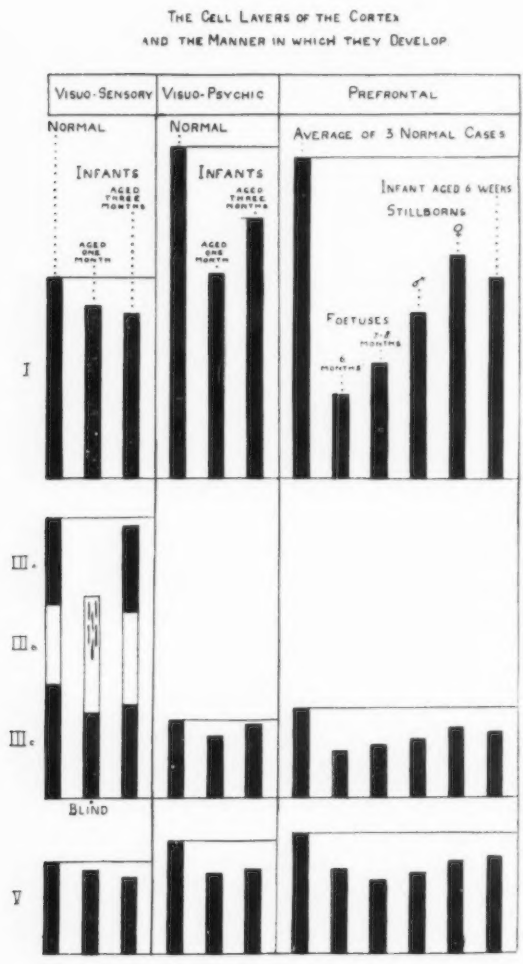

FIG. 21.

The figure shows the mode of evolution of the cell-laminæ of the cortex of the visuo-sensory, visuo-psychic, and prefrontal regions. The bottom series represents the inner cell- or polymorphic lamina, the middle series the middle cell- or granule-lamina, and the upper series the outer cell- or pyramidal lamina. A description is given in the text, but in general the figure suggests that the visuo-sensory cortex develops before the visuo-psychic, and this before the prefrontal; that the inner cell-lamina develops before the middle, and the middle before the outer; and, finally, that in the visuo-sensory and visuo-psychic regions the middle cell- or granule-lamina is the receptive lamina of the cortex and develops more rapidly than does the inner cell-lamina of these regions. The measurements from which this table is compiled, together with other details concerning the cases contained in it, are summarized in Appendix A.

the inner cell-lamina of this case is by no means so well developed. In other words, the granule- or receptive-lamina of the visuo-psychic zone follows the order of its evolution in the visuo-sensory area in being ahead of the inner cell-lamina in its degree of development.

In the case of the prefrontal region, though the results are not comparative, they are sufficient (especially when combined with other data to which I shall refer later) to indicate that evolution is individually variable, and occurs at a later date than is the case in either of the other two regions.

Chapter IV.

The Lamination of the Visuo-sensory Area, the Visuo-psychic Zone, and the Prefrontal Region.

I now propose to illustrate the lamination of the regions of the cortex which are under consideration, and in the case of the prefrontal area it is my intention, for reasons which I shall presently detail, to describe at some length its general structure. I would add that the microphotographs I am about to exhibit are of different magnifications, as it is necessary that the whole depth of the cortex should be present.

As the lamination of the visuo-sensory area is somewhat difficult to analyse without special experience, the first microphotograph (fig. 22) I shall exhibit is prepared from this area in the rhesus, in which the various laminæ are exceptionally well defined.

The layers shown in this specimen from above downwards are the outer fibre-lamina, or superficial layer; the outer cell-lamina, or pyramidal layer; the middle cell-lamina, which consists here of two granule-layers separated by the fibre-layer of Gennari, to which pass the terminal fibres of the optic radiations; the inner fibre-lamina, or inner line of Baillarger; and the inner cell-lamina, or layer of polymorphic cells.

In the next plate (fig. 23) is shown an average section of the same area in the normal adult. The same lamination is present, but it is more difficult to identify, and naturally still more difficult to measure.

[A photograph was shown illustrating the lamination of the visuo-psychic zone of the normal adult.] The five laminæ of which it is composed can readily be discerned. These are from above downwards the outer fibre-lamina, or superficial layer; the outer cell-lamina, or pyramidal layer; the middle cell-lamina, or granule-layer; the inner fibre-lamina, or inner line of Baillarger; and the inner cell-lamina, or layer of polymorphic cells.

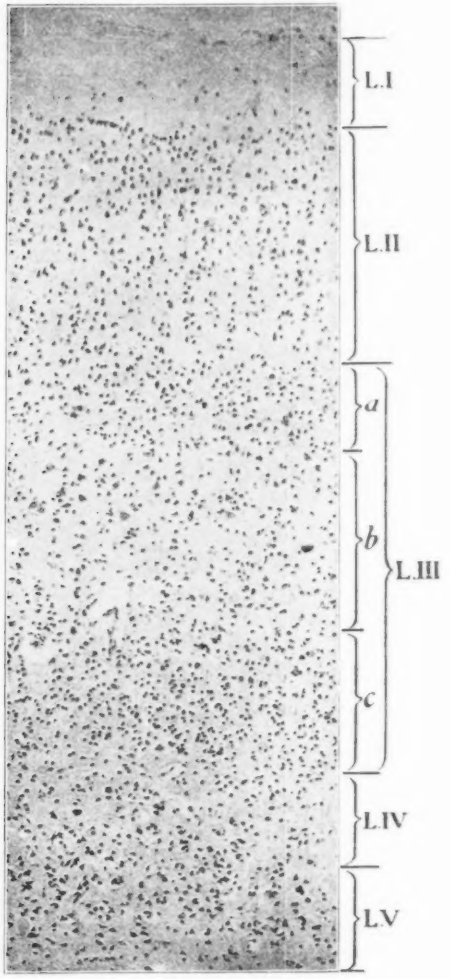

FIG. 22.

One hundred and nine diameters. The visuo-sensory cortex of the rhesus. I.L.I. the outer fibre- or superficial lamina. L.II, the outer cell- or pyramidal lamina. L.III, the middle cell- or granule-lamina, which is composed of two layers of granules, (*a*) and (*c*), separated by the horizontal fibre band of Gennari (*b*), in which terminate the fibres of the optic radiations. L.IV, the inner fibre-lamina or inner line of Baillarger. L.V, the inner cell- or polymorphic lamina.

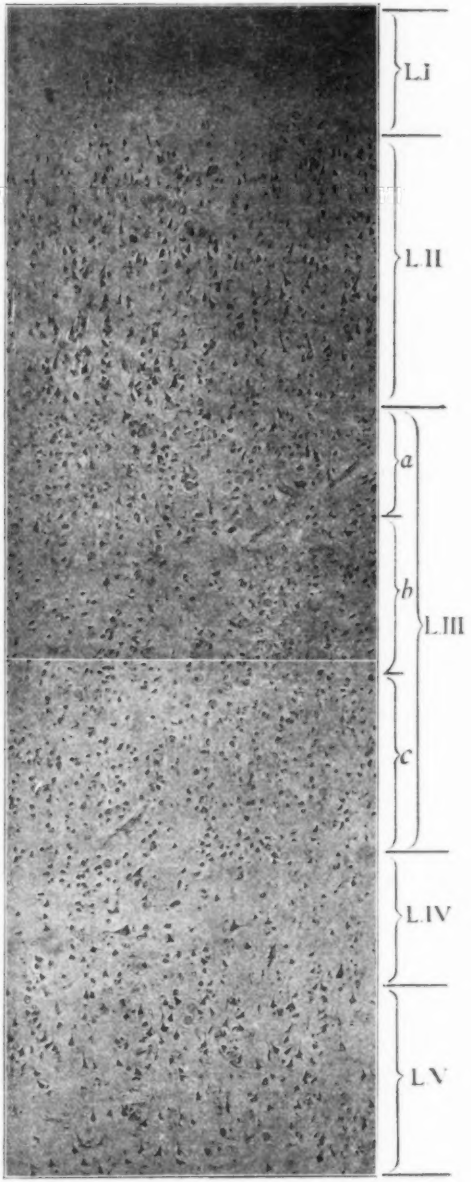

FIG. 23.

Ninety diameters. The visuo-sensory cortex of man. L.I to L.V, as in fig. 22. The lamination of the human visuo-sensory cortex is not easily recognized without special experience, but the different laminæ can be identified without difficulty if the figure be compared with the microphotograph of the visuo-sensory cortex of the rhesus, in which the various laminæ are very clearly defined.

[A photograph was also shown of a section through the periphery of the visuo-sensory area to display the manner in which the visuo-sensory cortex passes abruptly into the cortex of the visuo-psychic zone.] It will be seen that the line of Gennari suddenly ceases and the two layers of granules run into one, which occupies the site of the inner of these,

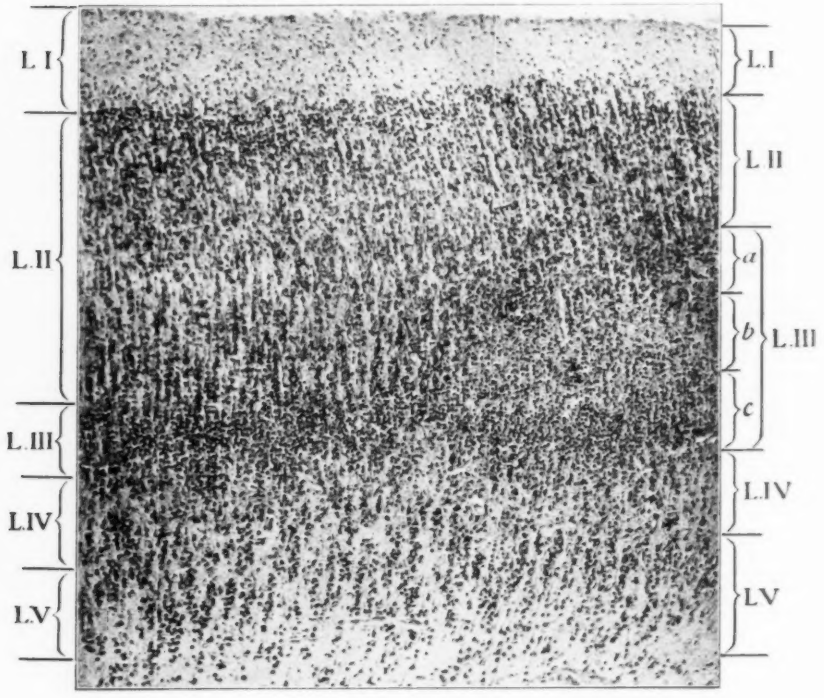

FIG. 24.

One hundred and nine diameters. The cortex of a seven to eight months' fœtus. The microphotograph is prepared at the periphery of the visuo-sensory area, and shows the passage of the visuo-sensory cortex into the visuo-psychic. L.I to L.V are as in the preceding illustrations; L.III*a* and L.III*c* are the two layers of granules, and L.III*b* is the intermediate fibre-layer or line of Gennari, of which three layers the middle cell-lamina consists in the visuo-sensory area. In the centre of the illustration it will be noted that the line of Gennari, L.III*b*, ceases, and that the layers of granules, L.III*a* and L.III*c*, run into one to form the granule-lamina, L.III, of the visuo-psychic cortex. A comparison of this figure with fig. 16, which illustrates the prefrontal cortex of the same case, very clearly demonstrates that the visual cortex of this case is much more advanced than that of the prefrontal region in its degree of development. These figures thus afford a partial graphic illustration of the truth that the visuo-sensory cortex develops before the visuo-psychic and the latter before the prefrontal.

the outer cell- or pyramidal lamina at the same time increasing to almost double the depth.

The same points are seen with perhaps greater clearness in the section (fig. 24) from a human fœtus of 7 to 8 months. A comparison of this illustration with an earlier one (fig. 16), which shows the prefrontal region of the same case, indicates that this last is in degree of development far behind the cortex of the visuo-sensory and visuo-psychic regions, which, particularly the former, much more closely resemble the adult type.

I think it quite certain that the outer layer of granules is the additional feature in the visuo-sensory area for three reasons: (1) The cortex normally evolves from within outwards. (2) The deeper layer of granules is of remarkably constant depth, almost as constant, in fact, as that of the inner cell-lamina, whereas the outer layer of granules exhibits differences in depth in individual cases, which are as readily determinable as are the corresponding differences that occur in the outer cell-lamina. (3) The delicate fibre-band in other parts of the cortex, which I personally regard as the homologue of the line of Gennari, is situated between the outer and middle cell-laminæ—i.e., above the granule-layer. This point is illustrated in the following rough diagram (fig. 25) of the fibre-bands of the cortex of the visuo-sensory and prefrontal regions.

I would remark that the general fibre-architecture of the cortex depends for its chief characters on the lamination and on the relative development of the cell-elements of the different laminæ. In other words, the arrangement of the fibres depends upon the position, size, and number of the pre-existing cells, and the fibres lie where there is room for them. In the fourth lamina, where cells are relatively few, a dense plexus of fibres exists and forms a definite horizontal band, the inner line of Baillarger or fourth horizontal fibre-band. This is particularly definite in the regions of association, but is usually invisible in a projection area like the visuo-sensory, since it is obscured by the immense number of projection fibres which traverse the cortex vertically to reach the line of Gennari. Between the second and third laminæ, where the larger pyramids are more or less definitely separated off from the subjacent granules, lies the third horizontal fibre-band or outer line of Baillarger, which in the visuo-sensory area contains the termini of the optic radiations and has received the name of "line of Gennari." In this region there is a great increase in the number of granules, a portion of which lies

Rough diagram of the
FIBRE BANDS OF THE CORTEX CEREBRI

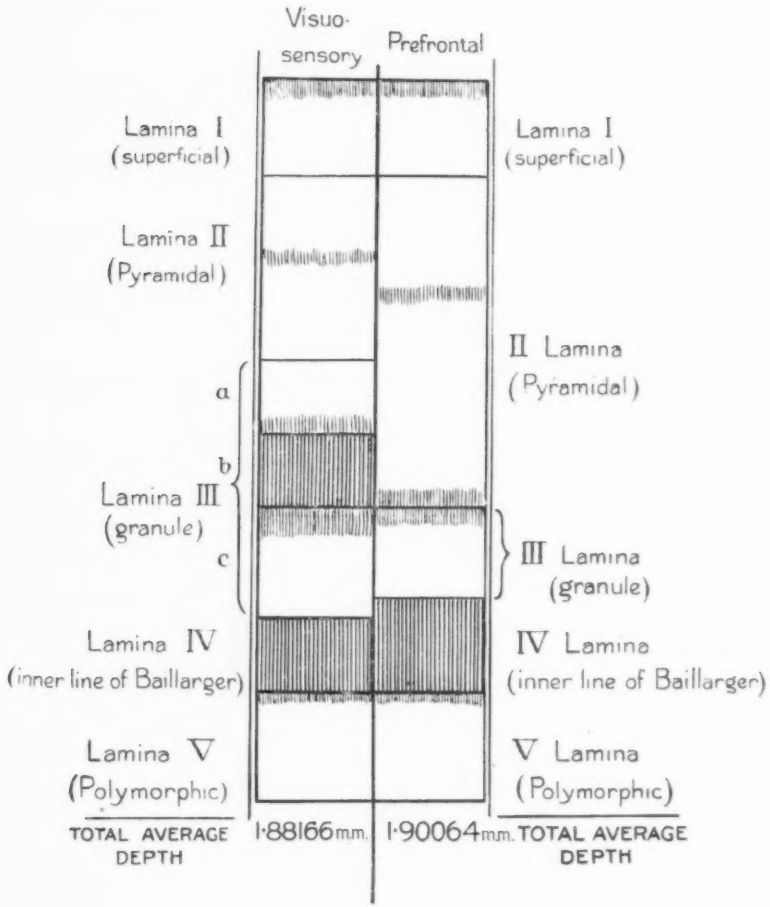

FIG. 25.

This diagram of the four horizontal fibre-bands of the cortex is not intended to show either the exact thickness of the bands, or the relative number of fibres contained in them. For the sake of simplicity, lamina I and V are made the same depth in the two regions. Of these four horizontal bands, the outer is the *layer of tangential fibres*, the next in order is the delicate *supra-radial band of fibres*, the next is the *line of Gennari* of the visuo-sensory area *and its homologue the outer line of Baillarger* elsewhere, and the innermost of the bands is the *inner fibre-lamina of the cortex or inner line of Baillarger*.

as a separate layer above this dense fibre-band and thus indicates its functional association with the third or granule-lamina. At about the upper trisection of the second lamina lies the thin second horizontal fibre-band or super-radiary plexus, and at the surface of the cortex lies the first horizontal fibre-band or layer of tangential fibres.

The horizontal fibre-bands of the cortex are thus a secondary and accidental feature dependent on the pre-existing cell-lamination, with the subdivision of which into laminæ they should not be confused.

Before proceeding to the consideration of the prefrontal[1] region, I wish to indicate my reasons for dealing with this in detail. As I shall indicate below, the prefrontal cortex is of great functional significance, and, in fact, constitutes the physical basis of the more general processes of cerebral association. It is the last region of the cerebrum to be evolved, its degree of evolution varies in normal individuals, and it is the first region to undergo dissolution in mental decadence. It is to be expected, therefore, that such a region should possess a structure of great delicacy and high complexity, and it would seem hardly necessary to demonstrate here that this is the case.

It has, however, been definitely stated by Campbell [10], in his recent monograph, which has attracted great attention, that the prefrontal cortex is of slight structural and functional significance. He remarks: "The structural development of the 'prefrontal' cortex is exceedingly low. It presents an extreme of fibre poverty. All the fibre elements are of delicate calibre, and its association system is particularly deficient. Its cell representation is on a similar scale. The cortex is also shallow." There is no mistake, as has been suggested, with regard to the region under consideration, as a comparison of the diagrams of Campbell and

[1] The "prefrontal region" may be defined as the anterior portion of the frontal lobe, including the mesial marginal gyrus but not the orbital surface. Its extent varies greatly in different brains. Its approximate fissural limitations are as follows: It is bounded laterally by the *inferior frontal sulcus;* and, anteriorly, by the *fronto marginal sulcus* of Wernicke (sulcus transversus anterior) at its inner part, and the *lateral fronto-marginal sulcus* of Eberstaller at its outer part. The convolutional pattern of the prefrontal region is approximately as follows: The *fronto-marginal sulcus* of Wernicke is often duplicated or triplicated, and that of Eberstaller may or may not have a *sulcus radiatus* above it. The anterior parts of the *superior and inferior frontal sulci* pass forwards over the prefrontal region. Between these is the *sulcus frontalis medius* of Eberstaller, which is often described as a sagittal and frequently detached part of the *fronto-marginal sulcus.* This sulcus is inconstant and often broken into pieces, and it frequently joins the *superior frontal sulcus.* In good brains it is well developed and lies in the centre of a large and complex *middle frontal gyrus.* Lastly, near the midline, parallel to the *superior frontal sulcus,* is the anterior portion of the inconstant and imperfect *sulcus mesialis* of Cunningham.

The prefrontal region as here defined approximately corresponds with the "prefrontal" cortex of Campbell (fig. 3), and with the corresponding histological region of Brodmann (10 of fig. 7). It is the site of the anterior centre of association of Flechsig (fig. 1). It is the chief focus of the sub-evolution and dissolution of the cerebrum which occur in amentia and dementia.

of Brodmann at once indicates; and I purpose showing that the cause of the great discrepancy in the descriptions of Campbell and myself lies in the difference of method adopted. Campbell used throughout his investigations the Wolters-Kulschitzky method, which, as ordinarily employed, I regard as quite unreliable for this especial purpose. The method, on the other hand, which I adopt for the staining of the fibres of the cortex, is based on the results of a research [5] which I conducted many years ago into the chemistry of the Weigert-Pal method. I found that this process is not a specific method for the staining of medullated nerve fibres with hæmatoxylin, but is a method of dyeing fibrils which comprises three distinct operations—the mordanting of the fibrils, the formation of a lake in them by the employment of a basic dye, and, finally, the removal of the stain by oxidation from nearly every other part of the complex tissue under treatment. I compared the method with what would occur were a fabric, composed of different fibres interspersed with fine glass threads, stained by a commercial process. The glass threads would refuse the mordant and consequently the lake, whereas the fibres would retain the stain. In the case of human tissue, the more highly metabolic elements represent the fibres, and the more fixed and lowly metabolic elements the glass threads. Further, the process is applicable to any, and not solely to nervous, tissue—e.g., kidney, involuntary muscle, &c., form beautiful low-power specimens. The mordanting of the tissue is the most important process, and osmic acid, iron alum, and ammonium molybdate (used separately or consecutively) are the strongest mordants. My results were independently and almost simultaneously confirmed by Herrick [12], and the method has for years been successfully applied to the staining of cortical fibrils by G. A. Watson [24], who, in 1903, published details of the special mode of employment necessary to display them, and of the difficulties which attend the obtaining of positive results. The usual Weigert-Pal methods, however, are still in general use, and by means of these it is practically impossible even imperfectly to stain the delicate fibrils of the prefrontal cortex.

Before dealing with the prefrontal cortex, I will now rapidly show a few slides illustrative of the results of the method I advocate :—

Fig. 26.—Medulla oblongata of frog, low power. Fig. 27.—Medulla oblongata of frog, high power. These two specimens are introduced in order to show the results of the method when applied to nervous tissue which is notoriously difficult to stain.

Fig. 28.—Posterior root ganglion of cat. This specimen demon-

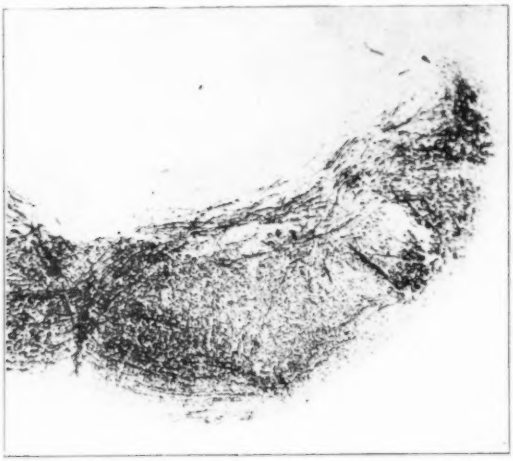

FIG. 26.

Thirty-seven diameters. Medulla oblongata of the frog. Mordanted with iron alum. The raphe is shown on the left of the figure. The nucleus near the upper surface at the outer trisection is shown, more highly magnified, in the next figure.

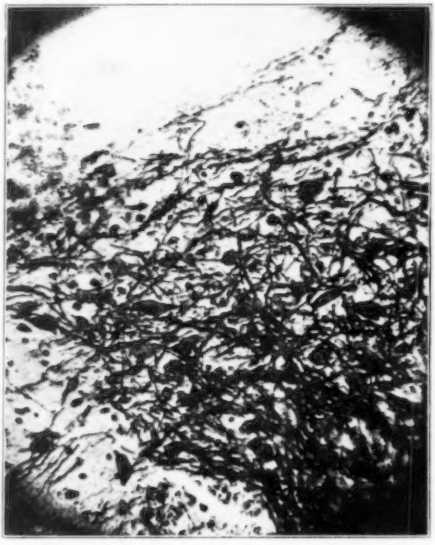

FIG. 27.

One hundred and fifty-seven diameters. Medulla oblongata of the frog. Mordanted with iron alum. The figure shows the nucleus referred to in fig. 26. The nerve-cells and the coarse and fine fibres are all intensely stained. The bodies in the upper part of the figure near the left-hand margin are red blood discs.

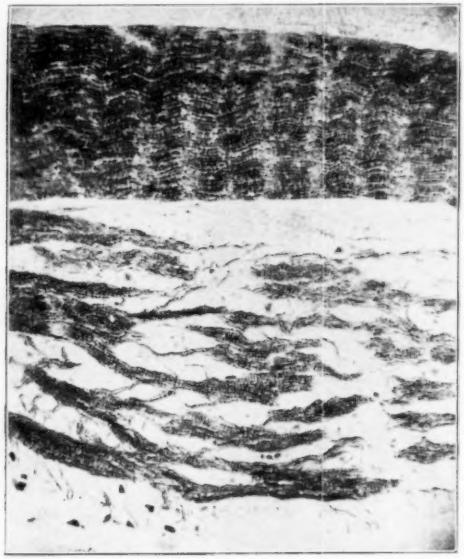

FIG. 28.

Thirty-two diameters. Longitudinal section of the posterior root ganglion of the cat. Mordanted with ammonium molybdate. The figure illustrates the results of the application of the method to ordinary coarse nerve fibres.

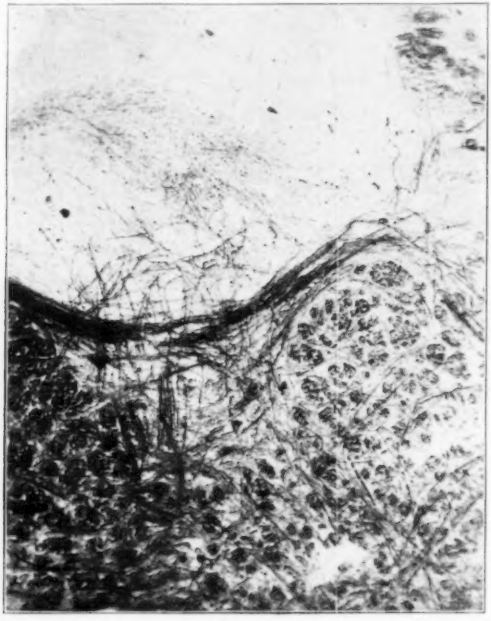

FIG. 29.

Fifty-eight diameters. Nucleus of origin of the hypoglossal nerve of the cat. Mordanted with ammonium molybdate. The figure shows the results of the application of the method to nervous tissue containing a plexus of delicate fibrils.

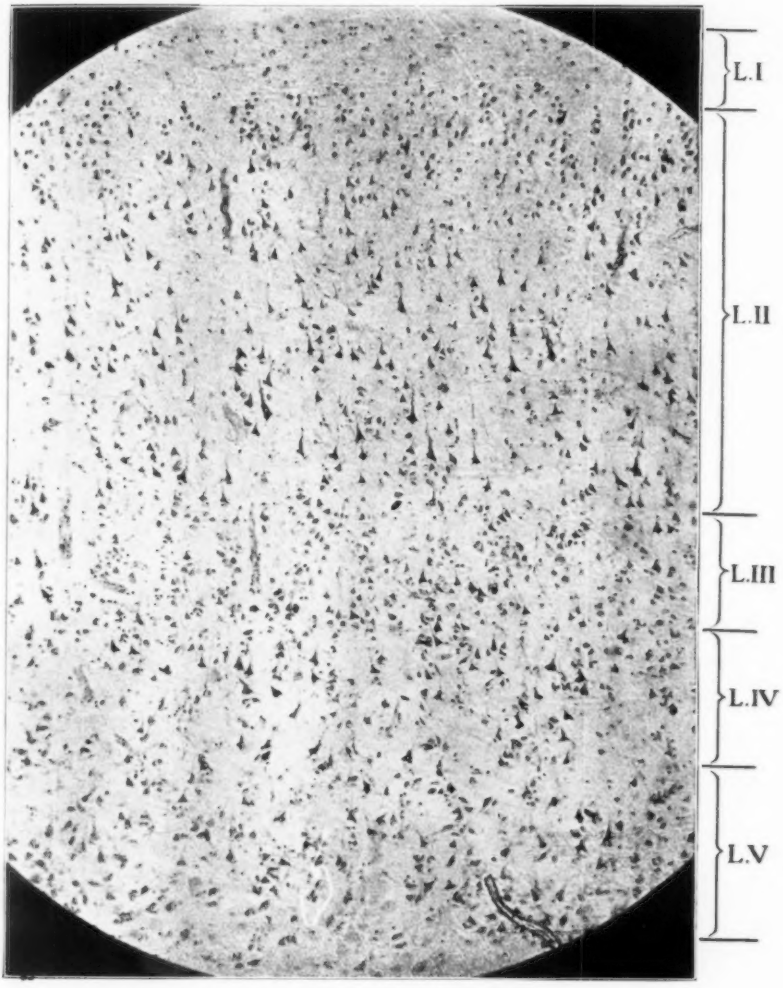

FIG. 30.

Eighty-two diameters. Normal prefrontal cortex of man. L.I to L.V as in previous figures. The figure gives a general view of the size, number, and degree of development of the constituent cells, which are well evolved even up to the surface of L.II.

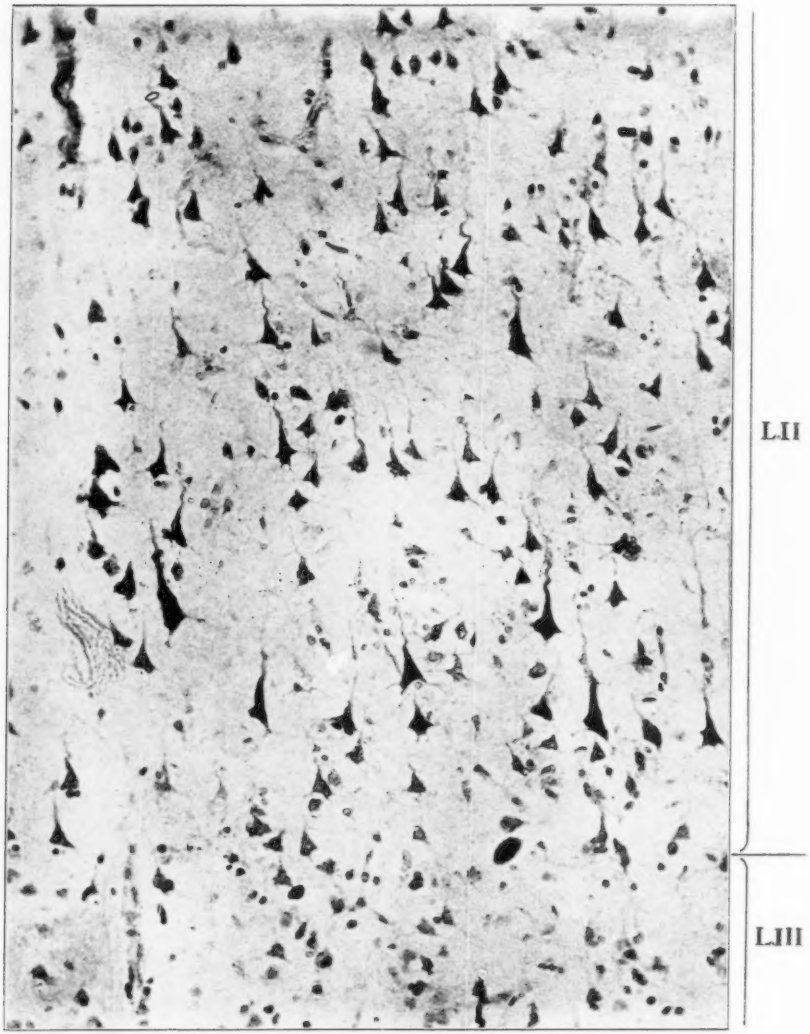

FIG. 31.

Two hundred and eleven diameters. A portion of the preceding microphotograph more highly magnified. L.I to L.V as in previous figures. The figure shows the lower two-thirds of L.II. and the upper portion of L.III. The well-known wavy appearance of the apical processes of certain of the cells, which is apparently due to some defect in the process of hardening, is well shown. Sections presenting this appearance are unsuitable for the purposes of measurement, however perfectly they may be stained.

strates the results of the application of the method to ordinary coarse nerve fibres.

Fig. 29.—Nucleus of the twelfth nerve: Cat. This photograph, on the other hand, shows the results of the application of the method to nervous tissue containing a plexus of delicate fibrils.

I will now pass to the consideration of the structure of the prefrontal cortex, and I would remark that the specimens from which I

Fig. 32.

Forty-eight diameters. A lower power microphotograph of the greater part of the depth of the cortex. The succeeding figures (figs. 33 to 36) show, from above downwards, parts of the cortex under a higher power; and a portion of the vessel which is seen below the centre of the figure appears in fig. 35.

have prepared the photographs were stained by G. A. Watson, and thus afford independent testimony with regard to the method and its results. As I have already remarked, the prefrontal cortex exhibits the same lamination as the visuo-psychic zone—namely, an outer fibre-lamina, outer and middle cell-laminæ, an inner fibre-lamina, and an inner cell-lamina.

The photograph on p. 65 (fig. 30), which includes the greater part of the depth of the cortex, gives a general view of the size, number and degree of development of the constituent cells, which are well evolved even up to the surface of the second lamina.

In the next (fig. 31), which is more highly magnified, the general appearance of the cells of the lower part of the pyramidal lamina is

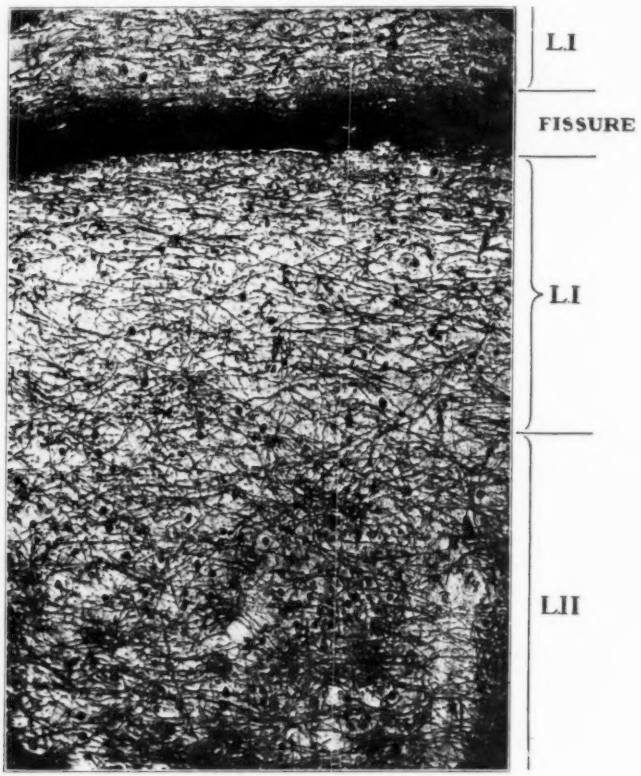

FIG. 33.

One hundred and sixty-five diameters. The figure shows the great wealth of fine fibrils present in L.I and in the upper part of L.II.

shown. These specimens exhibit no evidence of cell paucity. They show the well-known wavy appearance of the apical processes of certain of the cells, which is apparently due to some defect in the hardening

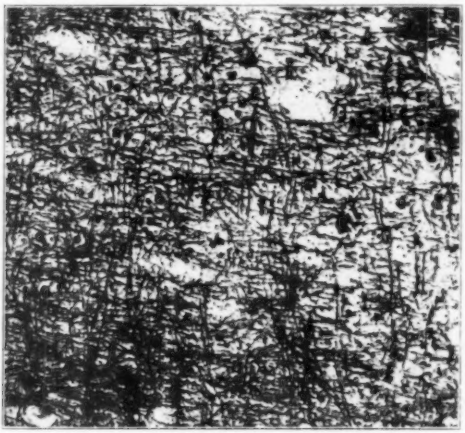

FIG. 34.

One hundred and sixty-five diameters. The figure shows the fibrillar meshwork which exists at the junction of L.II and L.III. In the upper half, the delicate horizontal feltwork above the granules may be seen.

FIG. 35.

One hundred and sixty-five diameters. The figure shows the fibrillar meshwork between the upper parts of the columns of Meynert. At the top of the figure is shown the lower part of the Λ-shaped vessel seen in fig. 32. To the left of the centre may be seen one of the relatively coarse vertical fibres which are present in considerable numbers.

process. For this reason I never employ sections, which exhibit this appearance, for the purposes of measurement.

I will now conclude this lecture by giving a few illustrations of the fibre architecture of the prefrontal cortex.

In the low-power photograph (fig. 32) the greater part of the depth of the cortex is included, and I shall show photographs of portions of this rom above downwards.

The first of these (fig. 33) shows the outer fibre-lamina or superficial layer. The fibrillar complexity is evident. In the lower part of the figure is seen the outermost part of the second lamina or pyramidal layer, and the fibre wealth is very clear.

The next (fig. 34) is taken at the junction of the second and third laminæ, and shows the delicate feltwork above the granules.

FIG. 36.

One hundred and sixty-five diameters. The figure shows six of the columns of Meynert, together with the feltwork of fibres between them.

The next photograph (fig. 35) gives the appearance of the cortex in the upper part of the columns of Meynert and includes a coarse nerve fibre which was visible in the low-power photograph.

The final specimen (fig. 36) is taken lower down, and shows the columns of Meynert.

In view of these photographs it is impossible to deny the great complexity of the fibre architecture of the prefrontal region; and I may add that John Turner [22], in 1906, almost simultaneously with the appearance of my paper on this subject, also combated the statements of Campbell and remarked that the prefrontal region, treated by a special method of his own, shows a wealth of intercellular fibrils probably greater than in any other region of the cortex.

CHAPTER V.

Intracranial Abnormal and Morbid Appearances in Mental Disease—Generalization of Amentia and Dementia.

Before proceeding to the consideration of the results of my investigation of the cortex cerebri of certain selected cases of insanity, I propose to refer briefly, from the clinico-pathological aspect, to certain abnormal and morbid appearances which are exhibited by the intracranial contents of the subjects of mental disease.

With few exceptions, which are unimportant in this connexion, such abnormal and morbid appearances have long been well known, but, at any rate up to the time when I published my first paper on the subject, no attempt, so far as I am aware, had been made to correlate these with any special symptomatology, and they had been described as common concomitants of the more chronic forms of insanity. Of these abnormal and morbid appearances, the more important are abnormal structure or wasting of the cerebrum, thickening and opacity of the pia-arachnoid, disease of the cerebral vessels, excess of intracranial fluid, subdural deposit, thickening of the dura mater, and abnormalities of the cranial vault.

In two consecutive series of 200 and 233 cases of mental disease [7], from which cases of general paralysis and special examples of gross lesion, &c., were excluded, and in which both the clinical and the post-mortem aspects presented by them were systematically recorded, I was able to determine that an important correlation existed between these.

The cases of the first series were divided pathologically into five convenient, though artificial, groups, namely:—

(1) Cases with or without abnormal, but without morbid, appearances.

(2) Cases with slight morbid appearances—namely, slight excess of intracranial fluid, slight thickening of the pia-arachnoid, which stripped rather more readily than natural, and slight or no cerebral wasting.

(3) Cases with morbid appearances of moderate grade—namely, intracranial fluid to the level of the tentorium, moderate thickening of the pia-arachnoid, which stripped readily from the hemispheres, and a moderate degree of cerebral wasting.

(4) Cases with marked morbid appearances—namely, intracranial fluid well above the tentorium, much thickening and opacity of the pia-arachnoid, which stripped very readily from the cerebrum, much wasting of the cerebrum, and, as a rule, marked disease of the cerebral vessels.

(5) Cases with gross morbid appearances—namely, very definite excess of intracranial fluid, much thickening and opacity of the pia-arachnoid, which stripped like a glove from the hemispheres, gross wasting of the cerebrum, and almost invariable affection of the cerebral vessels, which were usually greatly diseased.

On comparing the cases, from the aspect of symptomatology, with the post-mortem records, it was at once evident that these five groups corresponded, with a few exceptions which were readily explicable, with five artificial clinical groups, namely:—

(1) Cases without dementia.

(2) Cases with appreciable dementia.

(3) Cases with dementia of moderate grade—i.e., the ordinary chronic lunatic with moderate dementia.

(4) Cases of severe dementia.

(5) Cases of gross dementia.

Exactly similar results followed the study of the second and confirmatory series of cases, and I have since, for some years, been accustomed to prognose intracranial appearances with certainty, in all but the rare cases in which I have been uncertain as to the clinical state of the patient.

For reasons which I shall very briefly lay before you, I was hence able to subdivide cases of mental disease into two types—namely, (1) cases which, from the macroscopic post-mortem aspect, exhibited abnormal, no abnormal, no morbid, or slight morbid appearances; and (2) cases which exhibited morbid appearances of any grade of severity, and, in some instances, abnormal appearances also.

The former group from the clinical aspect I class under the term "amentia," which I employ to connote *the mental condition of patients suffering from deficient neuronic development:* and the latter under the term "dementia," which I use to signify *the mental condition of patients who suffer from a permanent psychic disability due to neuronic degeneration following insufficient durability.*

The subjects of amentia, therefore, as I shall suggest from the macroscopic and prove from the microscopic aspect, suffer from a more or less marked grade of sub-evolution of the cerebrum. The chief clinical varieties of amentia are low-grade amentia, or idiocy and imbecility with or without epilepsy, and high-grade amentia, which includes "moral," unstable, and excited cases, together with cranks and asylum curiosities, recurrent cases of all types, hysteria, epileptic insanity, and true paranoia and allied cases.

Before referring to the question of dementia, a further explanatory description of this mental condition is necessary. The word "dementia," and particularly the word "demented," are employed by alienists for different purposes. Some speak of demented patients recovering, others regard almost any reasonably quiet chronic case as demented, and others, again, deny the possibility of in any way whatever correlating psychic states and material conditions of the brain, and regard such as a form of confusion of thought. It is therefore necessary, in addition to defining the term, to indicate the commoner symptoms which are presented by patients suffering from dementia.

These, in brief, are as follows:—

General dulness and apathy, a loss of initiative, and an indifference to their surroundings; a marked degree of stereotypism of all the mental processes, and an inability to learn new acquirements; a mechanical method of performing known acquirements, a general stupidity and inability to understand when an attempt is made at correction of any kind, and a tendency to revert to accustomed modes of speech and action; finally, there is a tendency to the repetition of accustomed actions which often shows that these have been performed in the entire absence of intelligent volition.

This description, I may remark, in certain respects resembles that given by numerous experimental physiologists with regard to the motor exhibitions presented by certain lower vertebrates after removal of the cerebral hemispheres, and by certain higher mammals after removal of the frontal lobes.

The subjects of dementia, as I shall indicate both macroscopically and microscopically, suffer from a more or less marked grade of involution or dissolution of the cerebrum. I group such cases into a primarily neuronic class composed of senile, presenile, mature and premature types; into a progressive and secondary class which includes senile dementia associated with gross degeneration of the cerebral vessels, and, as the result of a special study, general paralysis also; and into a class of special varieties following sense deprivation, epilepsy, and cerebral lesions.

This generalization of amentia and dementia is a gross one, and, as I shall indicate shortly, is based on the fact that cases of mental disease exhibit a lesion of the cortex of the prefrontal region of the cerebrum, which lesion, in the case of amentia, is of the nature of a true sub-evolution, and, in the case of dementia, is of the nature of a true involution or dissolution.

I would remark that the existence of amentia does not preclude the

onset of dementia, that the necessary precursor of dementia is a more or less severe grade of mental confusion, and that mental confusion, when incited by temporary and removable causes—e.g., alcoholic excess—is often entirely recovered from.

Further, certain clinical indications are frequently though not constantly present which enable a prognosis to be made as to whether a given case of mental confusion is recoverable or will result in dementia. Again, it is certain that recoverable mental confusion may occur in persons possessing normal cerebra. Lastly, mental confusion followed by dementia more commonly occurs in cases with cerebra of normal or relatively normal development, though probably of deficient neuronic durability, than in cases with cerebra which exhibit some grade of sub-evolution. The generalization may, in fact, be made that the greater the grade of amentia the less is the tendency to dementia, not through a more normal durability of the cortical neurones of the former, but owing to the fact that cases of amentia so readily suffer from symptoms of mental alienation under any form of "stress" that as a rule little or no irreparable damage to the cortical neurones results.

The generalization of amentia and dementia, I may remark, does not cover the subject of special symptomatology, which, as I hope to indicate, but not yet to fully prove, depends on the degree of evolution of the cortex of the projection areas and zones of lower association of the cerebrum.

Of the abnormal and morbid intracranial appearances to which I am about to refer, the simplest, and that which is most readily determinable with accuracy, is the weight of the stripped cerebral hemispheres in the fresh state. In the following table (fig. 37) are classified under the five groups which I have indicated the weights of the stripped hemispheres from 417 consecutive and unselected cases of mental disease.

It is at once evident that the weights in all the groups are much below the average normal weight, which I have estimated from the recent statistics of Marchand [17]. I do not lay stress on this point, as Marchand's results were obtained from the brains of Hessians, although, if to the weights of Group III one added the 30 to 50 grm. which it is probable they have lost in consequence of wasting, they would come approximately up to Marchand's figures.

I would, however, indicate the obvious and important conclusion that the average weights of the hemispheres in Group III must, before wasting had occurred, have been considerably greater than those in

Groups I and II. The average weights of the hemispheres of Groups IV and V, in which severe and gross wasting had occurred, point to the same conclusion—namely, that the original weights in these groups must have been considerably greater than those in Groups I and II, since the loss of cerebral tissue in the former groups cannot average less than about 100 grm., and may be much more, in view of the large amount of intracranial fluid which is present.

I would remark that the first two groups include a small number of cases who might have recovered had they lived, and whose brain weights would tend to increase rather than to decrease the average. They also include a small number of idiots and imbeciles whose brain weights do not affect the average to an appreciable degree, some of them being much above it. The few epileptics scattered through the groups

Weights of stripped Hemispheres from 417 cases

	GROUP	MALES		FEMALES	
	Total number of cases	Number of cases	Average weight in grammes	Number of cases	Average weight in grammes
		NORMAL	589·0	NORMAL	534·0
I	61 No wasting	21	552	40	497
II	95 Somewhat wasting	21	564	74	485
III	90 Moderate wasting	31	560	65	482
IV	90 Marked wasting	38	511	52	456
V	75 Gross wasting	25	513	50	437

FIG. 37.

have also no important influence on the average weight. Whilst such cases might with theoretical advantage have been omitted, they have no practical influence on the average weights of the groups, and their inclusion avoids the necessity of interrupting the consecutive series. *The striking conclusion thus follows that the average brain weight of lunatics without intracranial morbid appearances is less than the original average brain weight of lunatics who exhibit such changes.*

In other words, the cerebra of Groups III, IV, and V have fallen from a higher original level of development than that to which those of Groups I and II have attained.

I now turn to the consideration of the abnormal and morbid appearances presented by these cerebra. The question of abnormal appearances requires for its solution the microscopic rather than the macroscopic method. For example, a case of idiocy which I examined, and in which the brain, though somewhat below the average weight, appeared to the naked eye perfectly normal, except for slight simplicity of the convolutional pattern, and a somewhat decreased development of the prefrontal region, gave, when investigated by the micrometric method, general average measurements which were almost identical with those obtained from a still-born female infant. It is, nevertheless, common to meet with small, and especially with simply convoluted and abnormally convoluted, cerebra in cases belonging to the first two groups, though it is extremely rare to meet with under-developed cerebra of average convolutional pattern which show a macroscopic decrease reasonably comparable with the marked wasting presented by cases of severe dementia. In such cases the macroscopic decrease (apart, of course, from lesions due to abnormal development of vascular or traumatic origin) occurs in the prefrontal region of the cerebrum.

The evidences of wasting presented by the cerebra of the insane are, on the other hand, almost as fit a subject for macroscopic as for microscopic study, since, perhaps in the majority of advanced cases the tendency to decrease in cortical depth owing to neuronic loss is to some extent neutralized, especially towards the surface of the cortex, by reparative proliferation of the non-neuronic elements.

The macroscopic relationship of the degree of wasting to the degree of dementia is on the whole very exact, and the regions of relative wasting can with practice be determined with considerable accuracy. This relationship is more constant in ordinary insanity than in general paralysis, owing to the more complete removal of the products of neuronic degeneration which has occurred at death, though, when cases of general paralysis live long enough, the macroscopic wasting occupies the same sites as, and is often even more pronounced than, is the case in ordinary gross dementia.

These regions of wasting, taken generally—for individual variations occur—are as follows:—

(1) The greatest amount occurs in the prefrontal region.

(2) The wasting is next most marked in the remainder of the first and second frontal convolutions. [In dementia paralytica, Broca's gyrus should, as a rule, be included here, and (2) and (3) should follow (4).]

(3) It is perhaps next most marked in the ascending frontal and Broca's gyri, though this grade should, in many cases at least, follow (4).

(4) It is next most most marked in the first temporal gyrus and the insula, and in the superior and inferior parietal lobules. In practically all cases it is more marked in the two former than in the two latter.

(5) It is least marked in the remainder of the cerebrum (including the orbital surface of the frontal lobes), particularly the inferio-internal aspect of the temporo-sphenoidal lobe and the posterior pole of the hemisphere.

I am of the opinion that exceptions to this general order are invariably due to vascular or traumatic causes, and should therefore be excluded from the ordinary and normal wastings of dementia.

I now give figures of a number of hemispheres in illustration of the abnormal and morbid appearances which I have indicated. They are chosen on clinical grounds, being from patients in whom I was interested and with whose mental condition I was very familiar.

Group I.

Female, aged 28, single. An imbecile of moderate grade. The youngest of a family of eleven. Normal until a severe fall at the age of 3 years, after which she had fits until the age of 13. Was never at school, but when 8 to 9 years of age could converse and go errands.

Cerebrum small and simply convoluted, and very asymmetrical. R.H. (fig. 38) 372 grm.: L.H. 414 grm.

Male, aged 24, single, labourer. Insanity with epilepsy. An only child. Was in standard vii. at the age of 12 years. Had a severe fall at the age of 14 years, which was followed by fits. Mental symptoms began at the age of 18 years.

Cerebrum of average size and pattern. L.H. 593 grm. (fig. 39).

Female, aged 35, single. A drunken prostitute with over fifty convictions. Excitable, unstable, cunning and very dangerous. A terror to the nurses owing to her violence and her unfounded accusations of ill-treatment.

Cerebrum large and of rather simple pattern. L.H. 618 grm. (fig. 40).

Female, aged 30, single, servant. Heredity of insanity. Alcoholism. Previous attack. Acute mania of non-confusional type. Death from cancer of the lung nine months after admission.

Cerebrum large and of very complex pattern. L.H. 645 grm. (fig. 41).

Group II.

Female, aged 22, married, housewife. Acute mania following confinement and associated with some confusion. Died from phthisis two and a half years

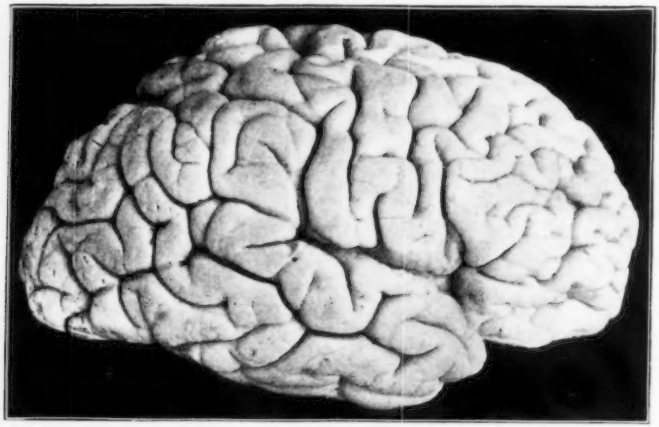

FIG. 38.

Right hemisphere of a female, aged 28. Single. An imbecile of moderate grade. Cerebrum small and simply convoluted, and very asymmetrical. R.H., 372 grm. L.H., 414 grm. No wasting. Group I.

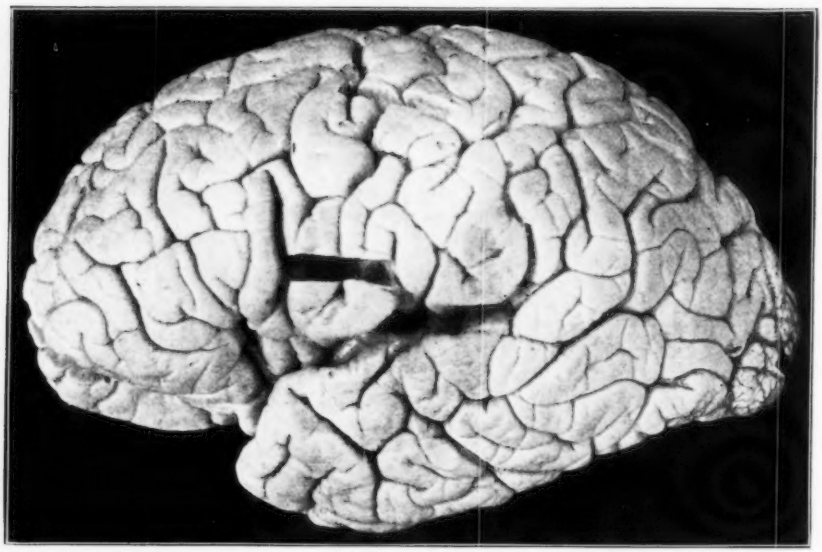

FIG. 39.

Left hemisphere of a male, aged 24. Single. Labourer. Insanity with epilepsy. Fits from the age of 14, and mental symptoms from the age of 18. Cerebrum of average size and pattern. L.H., 593 grm. No wasting. Group I.

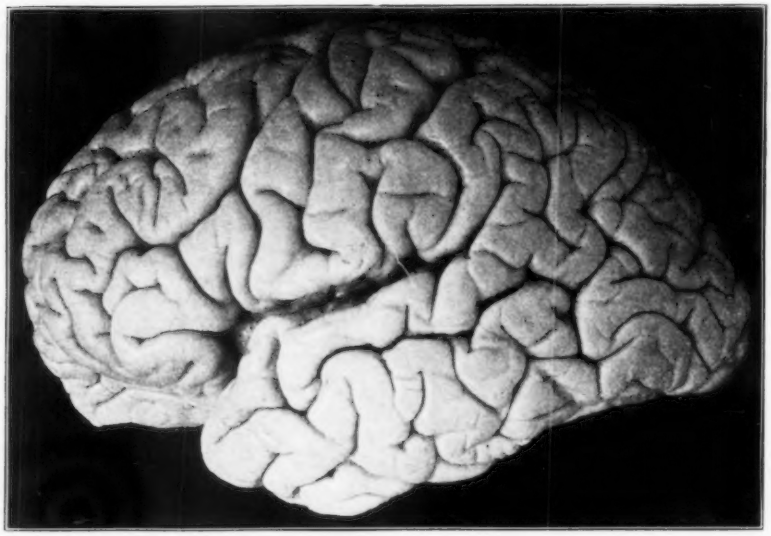

FIG. 40.

Left hemisphere of a female, aged 35. Single. A drunken prostitute with over fifty convictions. Excitable, unstable, cunning, and very dangerous. Cerebrum large and of rather simple pattern. L.H., 618 grm. No wasting. Group I.

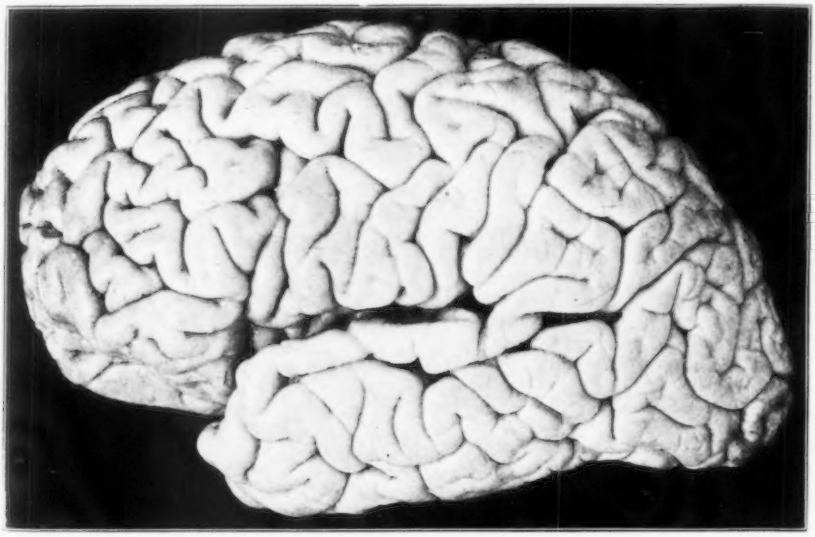

FIG. 41.

Left hemisphere of a female, aged 30. Single. Servant. Alcoholism. Acute mania of non-confusional type. Death from cancer of the lung nine months after admission (Case 7, Appendix B). Cerebrum large and of very complex pattern. L.H., 645 grm. No wasting. Group I.

after admission, and for some months before death exhibited well-marked stupor.

L.H. 495 grm. (fig. 42). Convolutional pattern was below the average in complexity. Slight intracranial morbid appearances.

Male, aged 52, married, steward. Mulatto. Intemperate. Slight dementia. Died, after a residence of 18 months, from aneurism of the aorta.

L.H. 520 grm. (fig. 43). Cerebrum below the average size, but little if anything below the average convolutional pattern. Slight intracranial morbid appearances, and slight prefrontal wasting. Moderate atheroma of cerebral arteries.

Group III-IV.

Male, aged 41, single, seaman. Duration of attack nearly 15 years. A case of chronic insanity who was at first depressed and confused. He then exhibited ideas of persecution, became grandiose, and eventually developed a moderate grade of dementia. Until he became demented he never spoke, refusing to communicate with others except by signs or by writing.

L.H. 525 grm. (fig. 44). Considerable wasting, chiefly in the prefrontal region. Several small softenings in the left hemisphere (cf. mental condition). Slight atheroma of the cerebral arteries.

Group IV.

Male, aged 61, single, schoolmaster. Duration 14 months. A case of melancholia with confusion which resulted in severe dementia.

Cerebrum large. Convolutional pattern very complex. L.H. 585 grm. (fig. 45). Marked general wasting, which is especially evident in the prefrontal region. Moderate degeneration of the cerebral arteries.

Group V.

Female, aged 78, widow, housekeeper. Duration about three years. A case of marked senile confusion. She was lost to time and place, and restless. She undressed herself. She suffered from illusions of identity. She developed gross dementia.

The cerebrum (figs. 46 and 47) had originally been probably of above the average size. R.H. unstripped, 525 grm. L.H. unstripped, 520 grm.; stripped, 480 grm. Gross cerebral wasting, which is especially marked in the prefrontal region. Some degree of asymmetry, the right hemisphere being of simpler pattern than the left. Gross degeneration of the cerebral arteries.

Gross Dementia Paralytica.

Male, aged 41. Heredity. Syphilis. Duration about two years. The case began with a long series of epileptiform convulsions and rapidly passed into gross dementia.

L.H., when partially stripped, 475 grm. (fig. 48). Wasting very extreme in the prefrontal region, and extreme in the rest of the frontal lobe, the first temporal

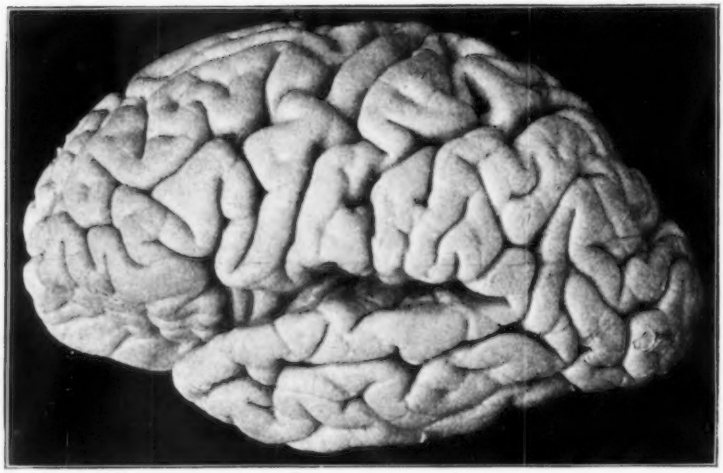

FIG. 42.

Left hemisphere of a female, aged 22. Married. Housewife. Acute mania following confinement and associated with some confusion. Died from phthisis two and a half years after admission; and for some months before death exhibited well-marked stupor. Cerebrum below the average size, and convolutional pattern below the average in complexity. L.H., 495 grm. Slight intracranial morbid appearances. Group II.

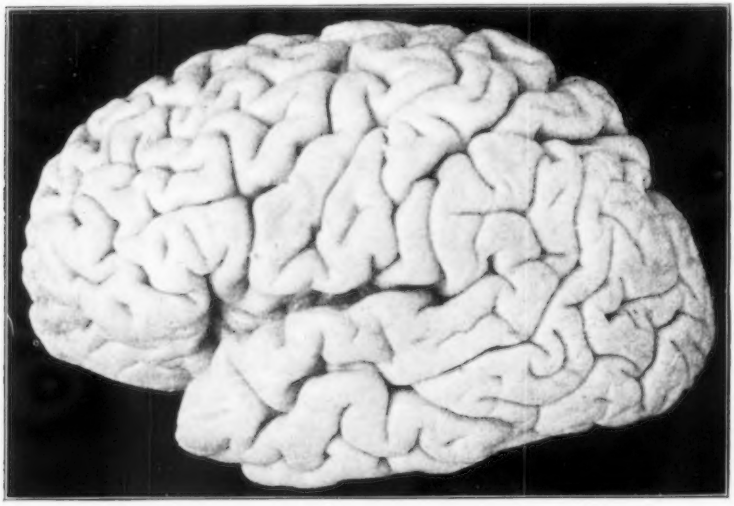

FIG. 43.

Left hemisphere of a male, aged 52. Married. Steward. Mulatto. Intemperate. Slight dementia. Cerebrum below the average size, but little, if anything, below the average convolutional pattern. L.H., 520 grm. Slight intracranial morbid appearances, and slight prefrontal wasting. Moderate atheroma of the cerebral arteries. Group II.

FIG. 44.

Left hemisphere of a male, aged 41. Single. Seaman. Duration of attack nearly fifteen years. Chronic insanity, with moderate dementia. Until the patient became demented he never spoke a word, refusing to communicate with others, except by signs or writing. L.H., 525 grm. Considerable wasting, chiefly in the prefrontal region. Small softenings at the hinder part of the supramarginal gyrus, at the foot of the precentral gyrus, and at the anterior extremity of the inferior frontal gyrus. Slight atheroma of the cerebral arteries. Group III to IV.

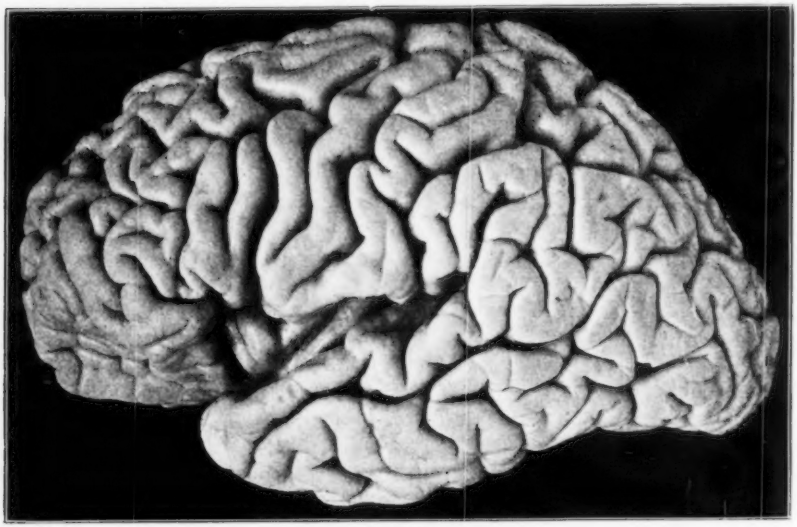

FIG. 45.

Left hemisphere of a male, aged 61. Single. Schoolmaster Duration fourteen months. A case of melancholia with confusion, which resulted in severe dementia. Cerebrum large. Convolution pattern very complex. L.H., 585 grm. Marked general wasting, which is especially evident in the prefrontal region. Moderate degeneration of the cerebral arteries. Group IV.

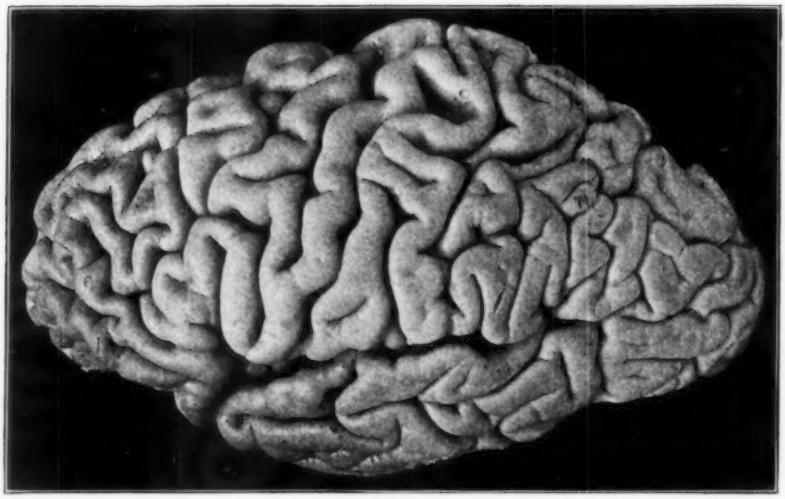

FIG. 46.

Left hemisphere of a female, aged 78. Widow. Housekeeper. Duration about three years. A case of marked senile confusion, resulting in gross dementia. The cerebrum had originally been probably of above the average size. R.H., unstripped, 525 grm.; L.H., unstripped, 520 grm.; L.H., stripped, 480 grm. Gross cerebral wasting, which is especially marked in the prefrontal region. Some degree of asymmetry. Gross degeneration of the cerebral arteries. Group V.

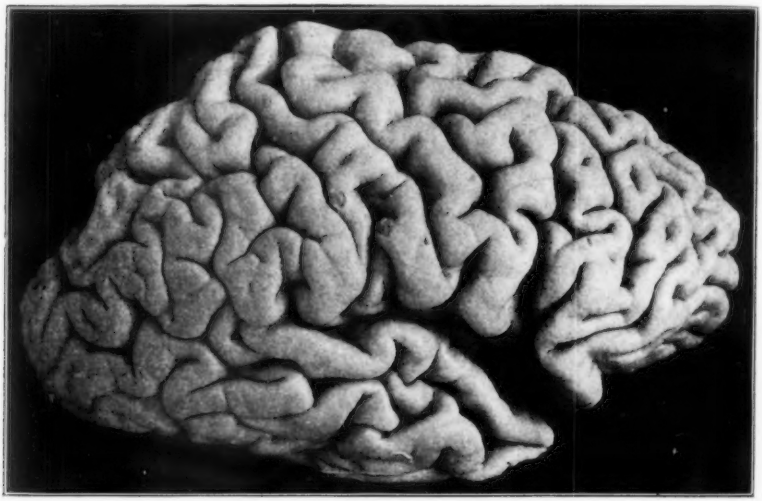

FIG. 47.

Right hemisphere of the same case. The pattern is simpler than is that of the corresponding hemisphere.

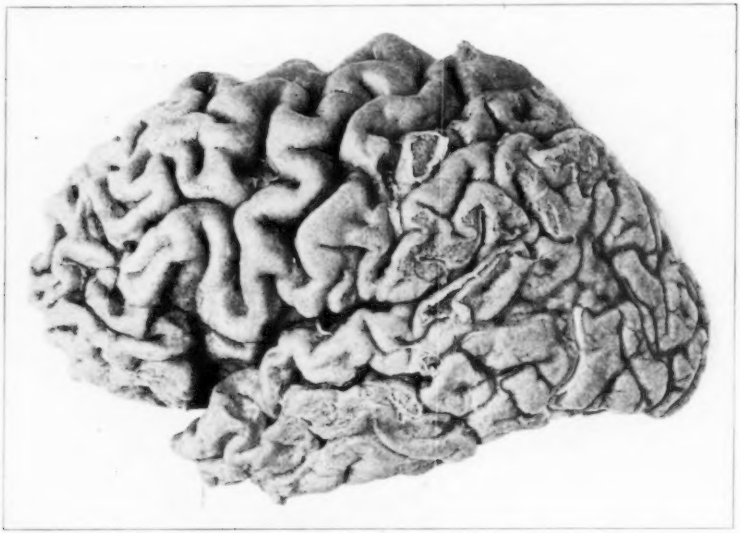

FIG. 48.

Left hemisphere of a male, aged 41. Heredity. Syphilis. Duration about two years. Gross dementia paralytica. L.H., when partially stripped, 475 grm. Very extreme prefrontal wasting. Extreme wasting of the rest of the frontal lobe, the superior parietal lobule, and the post-central and first temporal gyri. The acute degeneration, which in this particular case is indicated by the markedly adherent pia-arachnoid, is seen behind and below these regions.

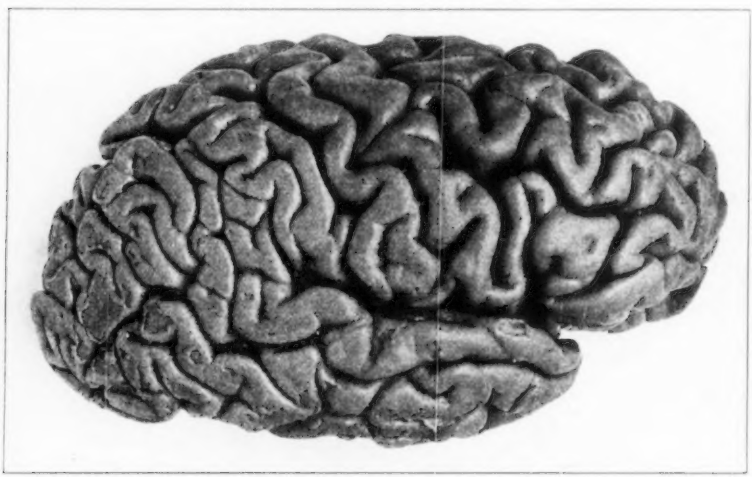

FIG. 49.

Right hemisphere of a male, aged 91. Senile decay, with relatively little dementia. Convolutional pattern somewhat above the average in complexity. R.H. 485 grm. Very gross degeneration of the cerebral arteries. The pia-arachnoid is grossly thickened over the fronto-parietal region, and adherent over the temporo-occipital. The hemisphere resembles that of Fig. 48 in the general distribution of the intracranial morbid appearances, but exhibits a marked contrast in the relative absence of cerebral wasting.

gyrus, the superior parietal lobule, and the post-central gyrus. Acute degeneration most marked in the outer part of the temporo-sphenoidal region, the inferior parietal lobule, and the preoccipital region.

Contrast Case.

Male, aged 91. Senile decay with relatively little dementia.

R.H. 485 grm. (Fig. 49). Very gross degeneration of the cerebral vessels. Piaarachnoid grossly thickened over the fronto-parietal region, and adherent over the temporo-occipital.

The case resembles the last in the general distribution of the different morbid appearances, but exhibits relatively little cerebral wasting, in this respect markedly contrasting with the previous case.

I will now draw your attention to the more important conditions which appear to influence the passage of cases from the earlier to the later groups, since, the groups being artificial, the position occupied by a particular brain at death depends on the grade of cerebral dissolution which has occurred when this ensues. Many cases remain in Groups I or II up to old age. These constitute the majority of the examples of low- or high-grade amentia of the types I have indicated. The remainder of these cases, often in consequence of severe poisoning of the cortical neurones (especially by alcohol), gradually pass into Group III, and eventually into the later groups. All the groups thus contain a number of examples of amentia.

The ordinary individual of relatively normal cerebral development is not especially prone to the onset of symptoms of mental alienation. When such a person becomes insane the limits of neuronic durability are as a rule passed, and the usual group into which the brain falls is the third, though the patient may die before it is reached. Group III, in fact, represents the position which would be eventually occupied by nearly all examples of cerebral dissolution, in the absence of the additional factor to which I am now about to refer—namely, degeneration of the cerebral vessels.

I have elsewhere shown that there is a direct relationship between the presence of degeneration of the cerebral vessels and the existence of advanced cerebral dissolution. That the latter is not a necessary consequence of the former is proved by the occasional existence of gross vascular degeneration without the co-existence of marked cerebral dissolution. Whilst both (in the absence of former syphilis) commonly occur in old age alone, neither is the necessary consequence of this, since senility, or the period at which the body-elements wear out, is an extremely elastic

term, depending on their inherent resistance and on the stress to which they are subjected.

The relationship between the presence of degeneration of the cerebral vessels and the development of dementia may be thus summed up: *In a cerebrum which has begun to break down, or where degeneration has progressed to the "moderate" stage (Group III), the presence or incidence of gross degeneration of the cerebral vessels will cause rapid progress of the neuronic degeneration, with, from the clinical aspect, gross dementia.*

The contents of Groups IV and V are thus examples of progressive and secondary dementia, and are, I may remark, homologous, in my opinion, with cases of general paralysis. In both these conditions neuronic dissolution and reparative reaction of the non-neuronic elements of the encephalon occur *pari passu*. In the case of dementia paralytica the latter is more or less intense, and vascular degeneration is relatively slight; in the case of progressive senile dementia the latter is relatively feeble, and vascular degeneration is relatively severe. I would illustrate this point by a coarse analogy, comparing dementia paralytica to certain types of progressive renal cirrhosis, and progressive senile dementia to senile renal cirrhosis.

Before proceeding to the consideration of the general histology of mental disease, I would remark that certain general bodily diseases may seriously modify the macroscopic appearances presented by the intracranial contents. Of these the chief is tuberculosis, which not only so modifies the clinical picture exhibited by many cases of mental disease as often to render accurate clinical diagnosis almost an impossibility, but by producing œdema of the intracranial contents occasionally makes the determination of the group to which the case belongs a question of great difficulty.

Chapter VI.

Micrometric Examination of the Cerebral Cortex in Mental Disease.

I now turn to the second part of my subject—namely, the description of the results of the micrometric examination of the cerebral cortex.

The series I am about to describe includes thirty cases, of which four are normals, and twenty-six are types of mental disease which grade from the idiot on the one side to the gross dement and gross general paralytic on the other. In twelve cases the visuo-sensory and visuo-psychic regions, and in seventeen cases the prefrontal have been

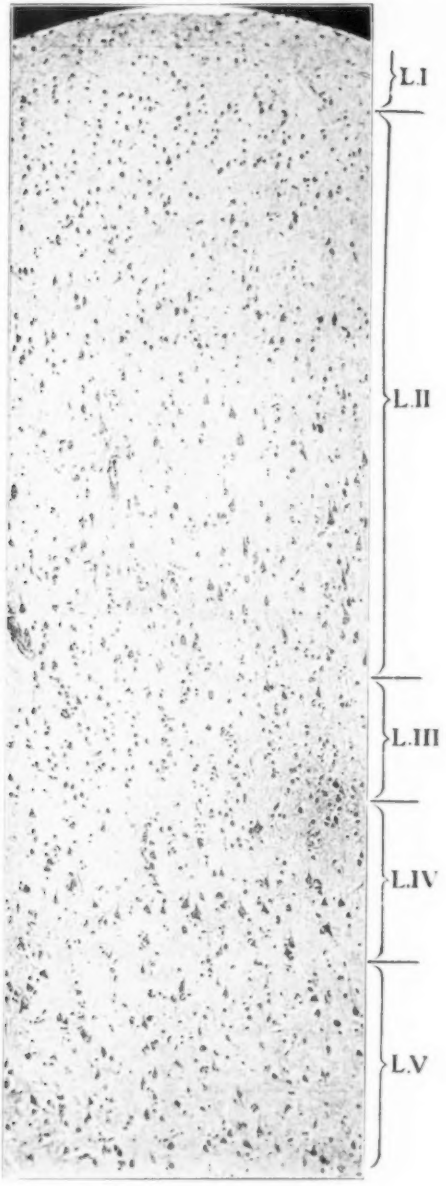

FIG. 50.

Seventy-six diameters. The prefrontal cortex of a normal adult. The magnification is somewhat less than is that of the succeeding figs. 51, 54, and 55. L.I to L.V as in previous figures.

examined and measured, whilst in one, to which I shall refer in greater detail, all these regions have been exhaustively dealt with. From the theoretical aspect, a series of cases in which all three regions had been studied would have been preferable. This, however, has not been possible, owing to the length of time occupied by the collection and examination of the material, and the great labour, and particularly the eye-strain, necessitated by such a method as that which I have been compelled to adopt. The micrometric study of the cortex by this

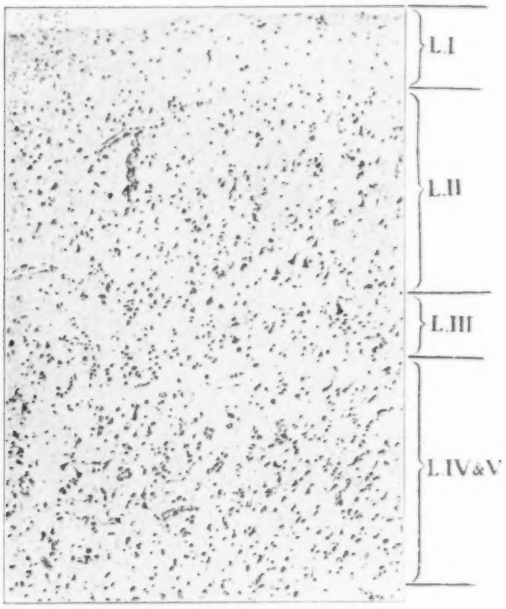

FIG. 51.

Eighty-four diameters. A case of severe imbecility (Case 14, Appendix B). L.I to L.V as in previous figures. The markedly subnormal depth, which is especially evident in L.II, may be seen when the figure is compared with fig. 50, the normal. The constituent cells are deficient in number, defective in structure, and irregular in position.

method produces, however, such trustworthy and comparable results that the larger number of cases which I have thus been able to examine has widened the scope of the research without impairing the validity of the conclusions which result.

Before dealing with actual measurements, I propose to show a number of photographs of the cerebral cortex (from the prefrontal

region), in illustration of the great differences which are presented by cases of different types. As I have already fully described the method of measurement, it is merely necessary to remark here that such illustrations cannot be regarded as in any way indicative of the general average measurements which result from systematic examination, since, by choosing suitable regions, it would be possible to produce the greater number of the photographs from nearly any single case in the series. In all, with the exception of the two high-power microphotographs, the magnification is the same.

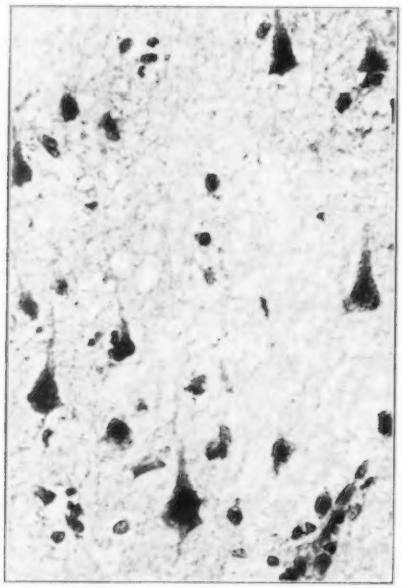

FIG. 52.

Three hundred and twenty-five diameters. Normal cells from the lower part of lamina II. The absence of the artefact seen in fig. 31 should be noted.

The first photograph (fig. 50) represents the normal appearance of the cortex. The five laminæ of which it is composed can readily be deciphered. I would particularly direct attention to the depth of the second lamina, or pyramidal layer, for comparison with the cases which follow.

In the next plate (fig. 51) is shown the cortex of a case of severe imbecility. The great decrease in depth, especially as regards the second lamina, is evident.

I now show, under a higher power, the cells of the lower part of the second lamina of this and of the preceding case. The first plate (fig. 52) shows the normal appearance of these cells, and the second (fig. 53) the stunted appearance and irregular position of the corresponding cells of the marked imbecile.

The next plate (fig. 54) shows the cortex of a well-marked imbecile of greater intelligence than the last case. The cortex is better evolved, and the larger cells are decently formed and less irregularly placed.

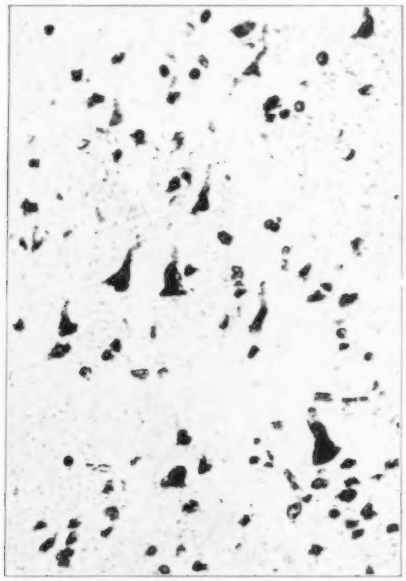

FIG. 53.

Three hundred and twenty-five diameters. Severe imbecility. The figure shows the stunted and irregularly placed cells from the lower part of L.II of the case illustrated in fig. 51. The contrast presented by the homologous cells of this and of the preceding figure should be noted.

[A plate was then shown to illustrate the cortex of an imbecile of still less marked grade.] The cortex of this case more resembles the normal, with the exception of lamina II, which is very narrow.

The next plate (fig. 55) shows practically the whole depth of the cortex of a case of gross dementia, this being very much shallower than the normal. The blood-vessels, I may remark, are both numerous and prominent when compared with a specimen of normal cortex stained

by the same method. The neuroglia cells are also very numerous in a section stained to show them.

Lastly, the final plate (fig. 56) of this series shows the approximate depth of the cortex in a fœtus of six months, a stillborn infant, a case of severe amentia, a normal adult, and a case of severe dementia.

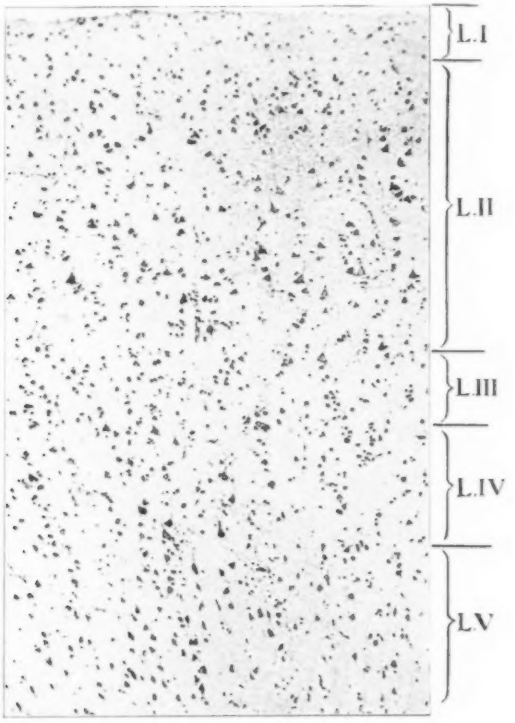

FIG. 54.

Eighty-four diameters. A case of well-marked imbecility (Case 15, Appendix B). L.I to L.V as in previous figures. The cortex is less markedly subnormal in depth than is that of the case illustrated in fig. 51, and the larger cells contained in it are less stunted in appearance, and also less irregularly placed.

Lines are drawn which include the second lamina and the third to the fifth laminæ, in order to show these more clearly.

I now come to the description of the results of the micrometric measurement of the cortex.

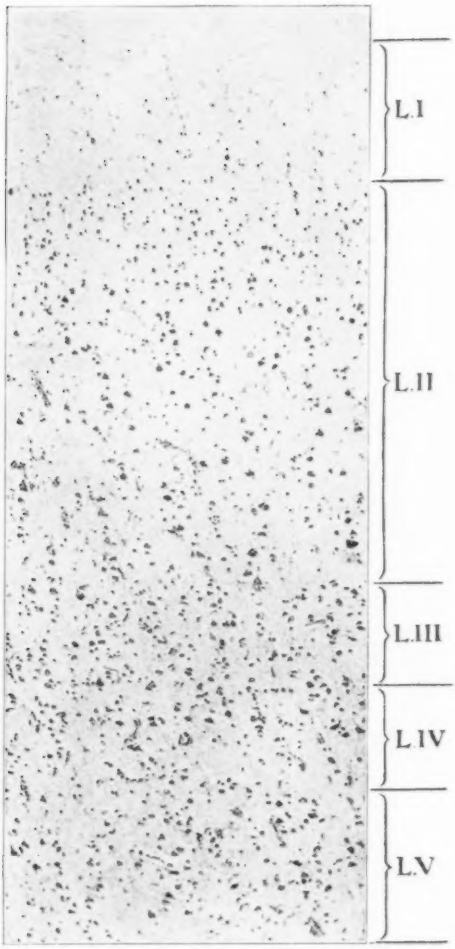

FIG. 55.

Eighty-four diameters. A case of gross dementia. (Case 29, Appendix B.). L.I to L.V as in previous figures. The cortex is much shallower than the normal. The constituent cells, particularly of L.II, are decreased in number and markedly diseased. Though this is not obvious in the figure, the blood-vessels are increased in number, and there is much proliferation of neuroglia, particularly in L.I and L.II.

I do not propose to describe the cases in detail, or to trouble you with actual figures, as I have already dealt in detail with the method I have adopted for the production of the general average measurements. I have therefore prepared the series of cases in percentages of the normal. I would remark that each case in itself represents the results of a small research, as the difficulties which have to be overcome in the preparation

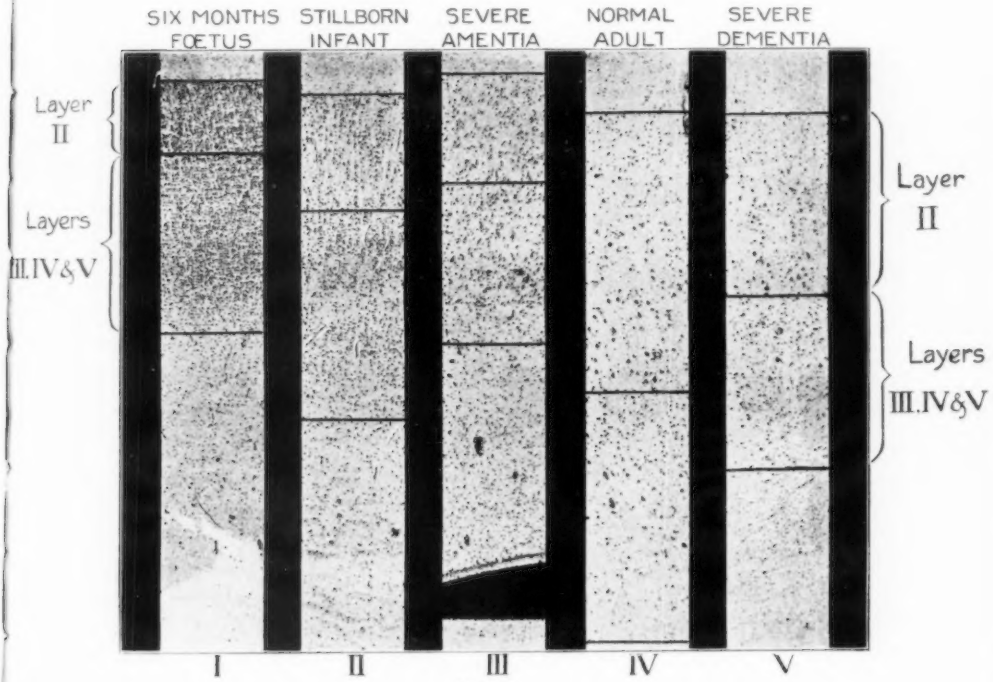

FIG. 56.

Forty-three diameters. The development of the prefrontal cortex and its condition in amentia and dementia. Horizontal lines are drawn to indicate lamina II, the pyramidal or associative lamina, and the combined III, IV, and V laminæ. A comparison of columns I, II, and IV indicates the relatively late development, and also the high degree of normal evolution of lamina II, compared with laminæ III, IV, and V. Column III indicates the marked sub-evolution of the cortex which exists in severe amentia, and column V the marked dissolution of the cortex which occurs in severe dementia.

of vertical sections, which include a sufficient number of measurable regions, are considerable even before it is possible to begin the measurements. In several instances it has in fact been necessary to reject a likely case owing to the impossibility of obtaining measurements, for

in some cases either every block which one cuts turns out to be more or less oblique, or else some particular region, especially the flat surface or the bottom, is either oblique or missing. I may add that several cases, when ready for measurement, have been of necessity rejected owing to the existence of cerebral œdema.

On the plate (fig. 57) are shown the general average measurements of thirty cases, grouped under visuo-sensory, visuo-psychic, and prefrontal regions. The cases are numbered to allow of identification, and those placed in the visuo-sensory and the visuo-psychic groups are the same.

The cases included in each group are arranged on each side of the normals, those of amentia rising in order of mental capacity from the left-hand side, and those of dementia falling in order of grade of dementia on the right-hand side.

The visuo-sensory group includes one idiot, two imbeciles, a case of imbecility with premature dementia, two cases of recent acute insanity, and a case of simple acute mania of nine months' duration on the left-hand side of No. 8, the normal; and a case of epileptic dementia, two cases of blindness with dementia, a case of premature dementia, and a case of well-marked dementia on the right-hand side of No. 8, the normal.

The visuo-psychic group contains the same cases.

The prefrontal group includes five cases of imbecility of different grades from severe to mild, three cases of recurrent and chronic insanity without dementia, three normal cases (the central one of which, No. 23, is taken as the basis for percentages), a case of imbecility with dementia, two cases of dementia of moderate grade, one case of well-marked dementia, No. 13, which is already included in the other groups, two cases of gross dementia, and one case of gross dementia paralytica.

In the visuo-sensory region the laminæ indicated are from above down the first or superficial layer, the second or layer of pyramidal cells, the third or granule layer, which is in this region duplicated and contains in its midst the line of Gennari, the fourth or inner line of Baillarger, and the fifth or layer of polymorphic cells. It is unnecessary at present to do more than draw your attention to the markedly decreased depth of the line of Gennari in the two blind cases, Nos. 10 and 11, which detail proves that the region under consideration is the projection area for visual sensations.

In the case of the visuo-psychic and prefrontal regions the laminæ indicated are, from above downwards, the first or superficial, the second or pyramidal, the third or granule, the fourth or inner line of Baillarger, and the fifth or polymorphic.

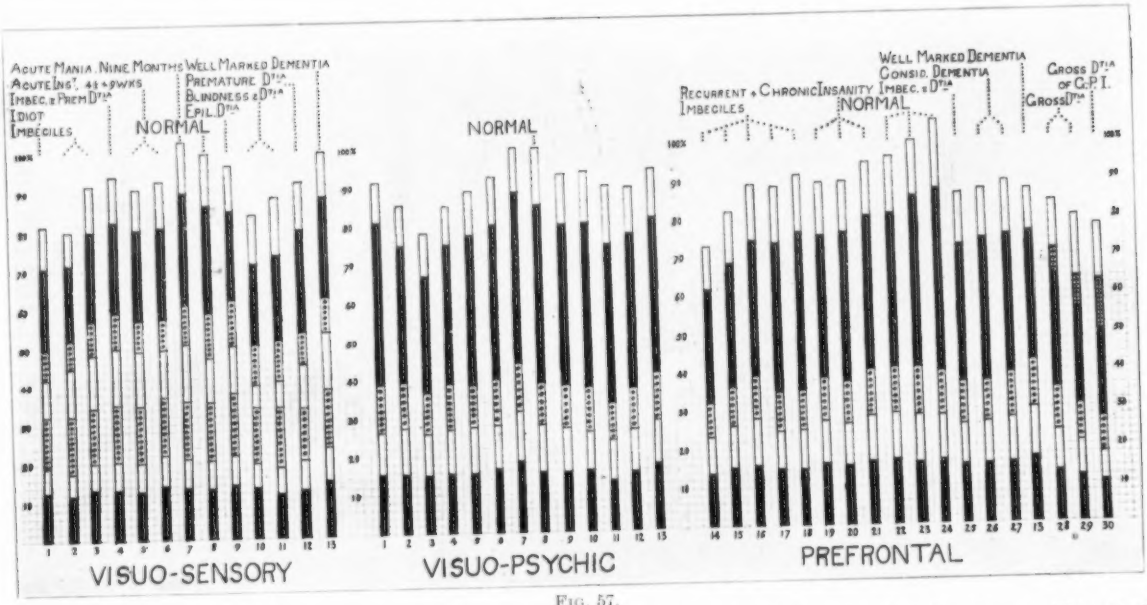

FIG. 57.

The general average depths, in percentages of the normal, of the cortices of thirty cases of various types. The actual measurements obtained from these cases, together with other details concerning them, are given or summarized in Appendix B. In the three series, the cases are grouped in each side of the normals according to the grade of amentia and dementia. The numbers at the bottom of the columns indicate the several cases. The sub-divisions of the columns from above downwards indicate the five laminæ of the cortex—namely, the outer fibre or superficial, the outer cell or pyramidal, the middle cell or granule, the inner fibre or inner line of Baillarger, and the inner cell or polymorphic. In the case of the visuo-sensory area, the receptive lamina consists of two layers of granules separated by an intermediate fibre-layer, the line of Gennari, in which terminate the optic radiations, and which is much decreased in depth in Nos. 10 and 11, the two blind cases. The figure shows that, whereas in the prefrontal region the cortex varies in depth according to the degree of amentia and dementia, no such variation occurs in the cases of the visuo-sensory and visuo-psychic regions. The further conclusions which are derived from a study of the individual cell-laminæ are indicated in fig. 58.

In the case of the gross dements, Nos. 28 to 30, in the prefrontal region, I would indicate that the depth of the outer two laminæ as measured is not an accurate criterion of the actual loss of neurones, owing to the proliferation of the non-neuronic elements which, especially in No. 30, is so marked as to a considerable extent to neutralize the results of neuronic destruction.

It is, of course, impossible to indicate the general conclusions which result from the study of these measurements without dealing with the cell layers individually. The most important result is, however, perhaps sufficiently evident to be worth pointing out.

Taking the prefrontal region first, it is obvious that in this region a definite relationship exists between the depth of the cortex of the respective cases and the degree of amentia or dementia which existed.

On the other hand, no such relationship exists in the case of the visuo-sensory and visuo-psychic regions, but an equally important conclusion may be drawn—namely, that great individual differences in depth are evident, in the former even more than in the latter; and that these individual differences not only bear no relationship to the degree of amentia or dementia which existed, but even in the case of the two regions differ in individual cases. The latter point is sufficiently evident if the first three cases are compared, since No. 1, an idiot, has poor visuo-sensory but good visuo-psychic measurements; No. 2, a well-marked imbecile, has equally poor visuo-sensory as but rather worse visuo-psychic measurements than No. 1; whilst No. 3, a moderate imbecile, shows fairly good visuo-sensory measurements but visuo-psychic which are much below those of either No. 1 or No. 2.

As the visuo-sensory region subserves the reception and the immediate transformation of visual sensations, and the visuo-psychic is concerned with associational functions which have a special visual hall-mark, it may be concluded from these measurements that marked individual differences exist with regard to both these capabilities in the case of different subjects. The measurements thus afford anatomical proof of a clinical truth, which is, I think, generally recognized, in spite of the difficulty which attends its satisfactory exhibition.

In view of the possible criticism that the ages of the patients might to some extent explain the differences in measurement, I would remark that these vary from eleven to seventy-eight years, and that I have endeavoured without success to trace even a possible suggestion of any relationship between age and measurement.

I will now pass to the consideration of the individual primary cell-

laminæ—namely, the second lamina or pyramidal layer, the third lamina or granule-layer, and the fifth lamina or layer of polymorphic cells. These, as abstracted from the last plate, I now show on fig. 58.

It will be convenient to consider first all the three regions together from the general aspect, and then to deal with each region individually.

In the case of the fifth lamina, it is evident that its depth in the visuo-sensory region is considerably less than—namely, about $\frac{1}{16}$ of—its depth in the visuo-psychic and prefrontal regions, whereas it is of exactly the same depth in the two last. Further, in the visuo-sensory region seven of the twelve abnormal cases reach to or above the normal line, whereas in the visuo-psychic region only five of twelve, and in the prefrontal region but three of fifteen, excluding, of course, the three normals, which all reach it. The fifth lamina, apart from the normal difference in depth, is thus slightly better developed in the visuo-sensory region than in the visuo-psychic, and is much better developed in both these than in the prefrontal. Further, in the prefrontal region alone does this lamina in the several cases exhibit a gradation in depth which varies according to the degree of amentia and of dementia. This lamina is the first to be evolved during the development of the cortex, and rapidly attains to approximately the normal depth. It is only reasonably below the normal depth in the prefrontal region of infants, well-marked imbeciles and gross dements, all of whom are unable to attend to the ordinary bodily functions, such as feeding, the calls of nature, &c. This lamina has been shown by G. A. Watson [25], as the result of his study of the cortex of the chief orders of the mammalia, to be the best developed and most important cell- layer of the neopallium. It is therefore impossible to avoid the conclusion that the inner cell-lamina is the fundamental cell- layer of the cortex, and that it is concerned with the performance of the instinctive in contradistinction to the receptive, the psychic, and the voluntary- psychic activities.

I now turn to the third lamina or granule-layer. This lamina is exceptionally developed and complex in the visuo-sensory area, consisting of two granule-layers with an interposed fibre-layer, the line of Gennari, in which terminate the optic radiations. In the visuo-sensory area the lower of the two layers of granules is normally much deeper than is the same layer in the visuo-psychic and prefrontal regions, whereas the upper is slightly deeper than that in the visuo-psychic, and of the same depth as that in the prefrontal region.

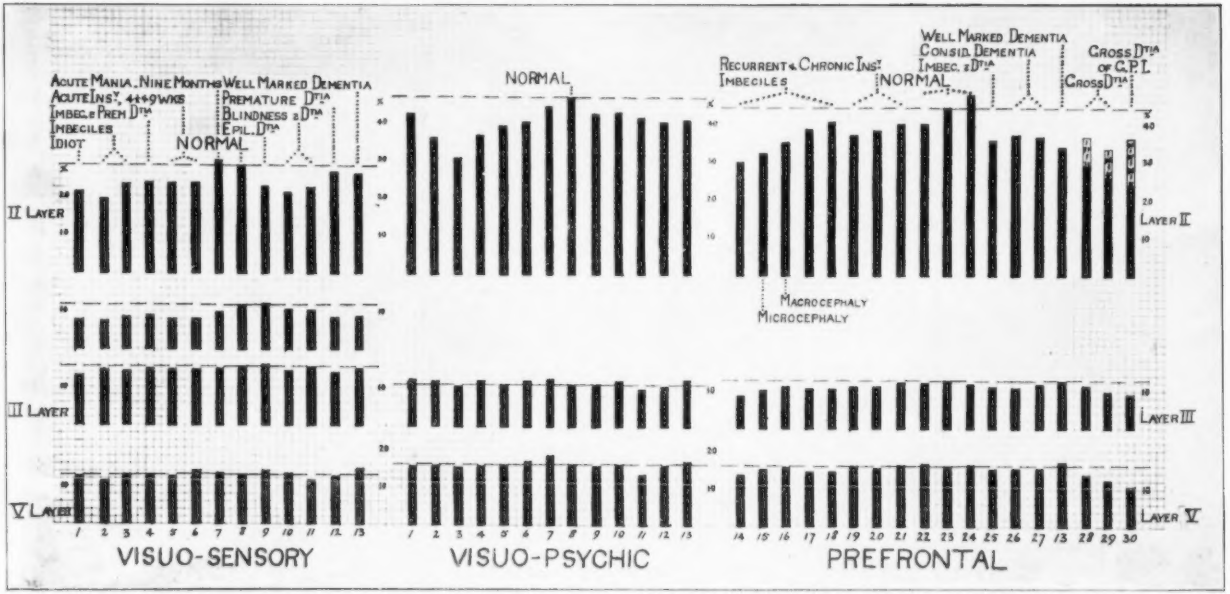

Fig. 58.

The outer, middle, and inner cell-laminæ of the thirty cases indicated in the last figure. (I) *The visuo-sensory area.* Specialization is marked, and is shown by the greatly increased depth and complexity of L.III, the middle cell- or receptive lamina, and by the much decreased depth of II, the associative lamina, and the decreased depth of L.V, the instinctive lamina. Well-marked individual variation occurs in the cases of the outer cell- or pyramidal lamina and the outer of the two granule-layers. In this region the cortex does not vary in depth according to the degree of amentia and dementia. (II) *The visuo psychic region.* Specialization is not marked, but is indicated by the well-developed L.III, or granule-lamina, and also by certain facts of evolution mentioned in Lecture II. Individual variation is well marked in the case of the outer cell- or pyramidal lamina. The cortex does not vary in depth according to the degree of amentia and dementia. (III) *The prefrontal region.* Indications of specialization and individual variation are practically absent. All the cell laminæ vary in depth according to the degree of amentia and dementia, and this variation takes place according to the order of normal development, L.V, the first to appear, being the least affected, and L.II, the last to appear, being the most affected. In amentia, therefore, the condition is one of true sub-evolution, and in dementia one of true dissolution or involution. In the case of Nos. 28 to 30, the decreased depth shown in L.II, and to some extent in L.III, is not indicative of the actual amount of neuronic loss, owing to the existence in these cases of more or less extensive reparative proliferation of the non-neuronic elements of the cortex.

Of these two layers of granules in the visuo-sensory area, both in the series of cases reach the normal depth in only one instance, and the lower layer is throughout much better evolved than the upper. In the visuo-psychic area, the granule lamina reaches up to or above the normal depth in nine of the twelve cases. On the other hand, in the prefrontal region, it is uniformly below the depth of the highest of the three normals in all the cases, and well exhibits a gradation according to the degree of amentia and dementia. Being the lamina, which is exceptionally evolved in the projection zones of the mammalian cortex, and being thus the layer which is especially concerned with the immediate transformation of afferent impressions, it is interesting to note the great variation in the degree of evolution of this lamina in the visuo-sensory region of the series of cases, and also that this variation is greater in the outer layer than the inner. I would further point out its relatively normal evolution in the visuo-psychic series, and its subnormal depth in the prefrontal series.

It is, I think, easy to arrive at a reasonable explanation of these differences in degree of development.

As I have already pointed out, the cortex of the visuo-sensory area is evolved earlier than that of the visuo-psychic, and this earlier than that of the prefrontal. It is therefore probable that in the case of the visuo-sensory area, the individual differences in the middle cell- or receptive lamina are indicative of individual differences in the functional capability of this lamina in different persons. On the other hand, in the prefrontal region the corresponding differences in the middle cell-lamina are simply greater in degree than are those in the inner cell-lamina, and less than are those in the outer cell-lamina, and are therefore due to the fact that the cortex of this region is as a whole in a condition of sub-evolution or dissolution according to the grade of amentia or dementia.

In other words, the granule-lamina of the visuo-sensory cortex exhibits considerable individual differences in its degree of evolution in different persons; the granule-lamina of the visuo-psychic cortex does not, being usually developed up to or above the particular normal with which they are compared; and the granule-lamina of the prefrontal cortex exhibits degrees of sub-evolution and dissolution which are part of the sub-evolution or dissolution of the whole cortex which occurs in this region alone, and varies in degree according to the existing grade of amentia or dementia.

I will now deal with the second lamina or pyramidal layer. This lamina passes the normal in one case in the visuo-sensory region, and in

one of the three normal cases in the prefrontal region. In no other case does it reach the normal depth. In the visuo-sensory region it is in some cases better, and in others worse, evolved than in the visuo-psychic region. These differences bear no constant relationship to the degree of amentia or dementia. On the other hand, in the prefrontal region, the depth of this lamina varies directly according to the degree of amentia or dementia present. In normal evolution this lamina is the last of the cortical laminæ to be evolved, and it develops in the visuo-sensory area earlier than in the visuo-psychic, and in the visuo-psychic earlier than in the prefrontal region. It is poorly evolved in the lower mammalia, but rises in its degree of development during the ascent of the mammalian scale, as has been shown by G. A. Watson [25] and by Brodmann [9]. It is therefore concerned with the psychic or associational, in contradistinction to the instinctive, activities of the cortex. From the table of measurements it may be concluded that these are in man pre-eminent and voluntary in the prefrontal region, that they are of less general but of more specialized significance in the visuo-psychic region, and that they are of much less but nevertheless very specialized significance in the visuo-sensory area, in which the second lamina is normally but five-ninths of its depth elsewhere. Further, the individual variations in depth in the visuo-sensory and visuo-psychic regions of the series of cases point to real individual differences in the specialized functional capabilities of these regions, whereas in the prefrontal region the differences are not of an individual nature, but vary according to the degree of amentia or dementia which existed.

To turn finally to the general consideration of the cortex of each of these regions, I would again remind you that in normal evolution the visuo-sensory cortex develops before the visuo-psychic, and the visuo-psychic before the prefrontal, and also that the inner cell- lamina is evolved before the middle, and the middle before the outer. In view of these facts it is evident from the study of the different series of cases that the visuo-sensory cortex is rather better evolved and much more specialized and individually variable than the visuo-psychic; that the visuo-psychic is better evolved than the prefrontal, and that it also exhibits well-marked indications of specialization, and especially of individual variation; and that the prefrontal cortex shows clear indications, not of specialization and individual variation, but of sub-evolution or dissolution according to the grade of amentia or dementia. I would also indicate that, as the three normal cases show, the degree of its evolution varies considerably in normal individuals.

In the case of the visuo-sensory area, the specialization is indicated by the great depth and complexity of the third or granule-lamina, by the much decreased normal depth of the second or pyramidal lamina, and by the somewhat decreased normal depth of the fifth or polymorphic lamina, whilst the individual variation is chiefly visible, though not necessarily in the same direction or to similar degrees, in the outer granule-layer and the second or pyramidal lamina.

In the case of the visuo-psychic region, the specialization is indicated by facts of normal evolution which I have already pointed out, and by the well-developed third or granule-lamina; and the individual variation is especially evident in the second or pyramidal lamina.

In the case of both regions it may be added that, specialization being allowed for, whether the cases are considered individually or collectively, the degrees of evolution of the laminæ follow the normal order, the inner cell-lamina being better developed than the outer or middle.

In the case of the prefrontal region, whether the cases be considered individually or collectively, there is direct evidence of degrees of sub-evolution according to the grade of amentia, and of degrees of dissolution according to the grade of dementia. Further, this sub-evolution or dissolution involves the whole cortex, and this according to order of normal development, the inner cell-lamina exhibiting the least decrease and the outer the most.

Lest this should be doubted by any statistician, on the ground that the layers are not of the same depth and that, therefore, exact comparison is not possible, I have, in fig. 59, averaged together the depths of the laminæ of the various types of case, and turned these depths into percentages so that each lamina appears of the same depth. It will be seen that the inner cell-lamina is the first to be evolved and the outer cell-lamina the last; that the same order of sub-evolution applies according to the grade of amentia which existed; and that, in the case of dementia—also according to its grade—the outer cell-lamina, which is the last to be evolved, is the first to undergo dissolution, and the inner cell-lamina, which is the first to be evolved, is the last to undergo dissolution.

I will now complete this part of my subject by describing a special case in which I have exhaustively examined all the three regions under consideration. As far as it is possible to judge, the patient, before his illness, possessed at least the average normal degree of intelligence, and probably more. In the course of less than two years he gradually developed a well-marked grade of dementia, which was unusually profound

PERCENTAGES OF AVERAGE DEPTHS, IN THE CASES OF LAYERS II, III & V, ALL TO THE SAME SCALE IRRESPECTIVE OF ACTUAL DEPTH.

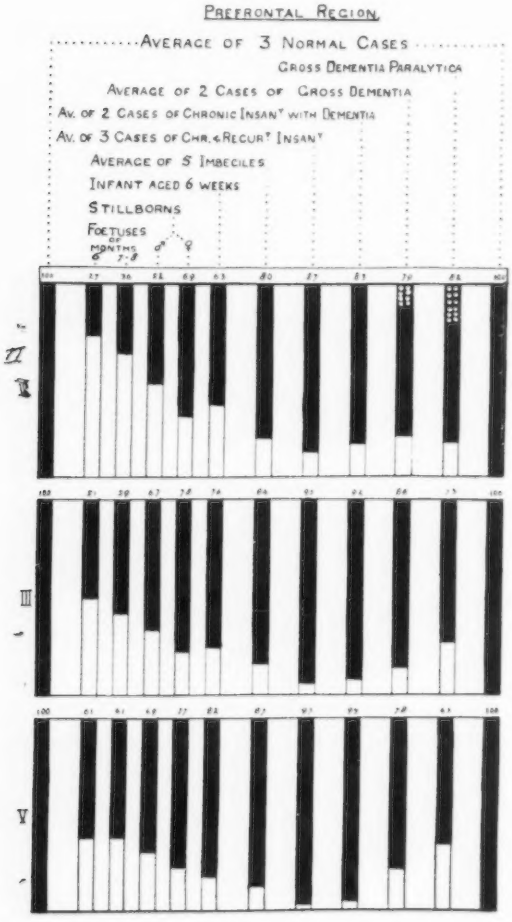

FIG. 59.

In this figure, for the purpose of direct comparison, the three cell-layers, of the prefrontal cortex of the cases which have been dealt with, are averaged into percentages of the normal, irrespective of actual depth. The figure proves that the inner cell-lamina develops before the middle, and the middle before the outer; that the same order of sub-evolution occurs in amentia; and that in dementia, if non-neuronic reparative proliferation in laminæ II and III be allowed for in the gross cases, the last lamina to develop is the first to undergo dissolution, and the first the last.

for a man of 44 years of age, who did not suffer from degeneration of the cerebral arteries. The cerebral dissolution was therefore of an unusually pure neuronic type; and it seemed to me, in view of the originally good development of the brain, that a better case could not well be found for the exhibition of the different grades of cerebral dissolution which might be expected to be found on examination of the visuo-sensory, visuo-psychic, and prefrontal regions of the cortex, since it was probable that all these, in their original condition, were of at least the average normal depth.

The results justified my expectation in that they showed quite clearly that the order of dissolution is the converse of that of normal evolution, the loss being most marked in the prefrontal region, next marked in the visuo-psychic zone, and least marked in the visuo-sensory area.

The results of the examination of this case are shown in the following diagram (fig. 60), in which are contrasted, in percentages of the normal, the general average measurements of the visuo-sensory, visuo-psychic, and prefrontal regions.

From the aspect of total depth, the visuo-sensory cortex is normal, the visuo-psychic shows a decrease of 6 per cent., and the prefrontal one of 13 per cent.

When the laminæ are individually considered there is, in the case of the outer cell-lamina or pyramidal layer, a 6-per-cent. decrease in depth in the visuo-sensory area, a 13-per-cent. decrease in depth in the visuo-psychic region, and a 24-per-cent. decrease in depth in the prefrontal region.

The middle cell- or granule-lamina is much below the normal in the visuo-sensory area, it is well above the normal in the visuo-psychic zone, and it is of practically the normal depth in the prefrontal region.

The inner cell- or polymorphic lamina is considerably above the normal depth in the visuo-sensory area, and is well above it in the visuo-psychic and prefrontal regions.

Whilst it is impossible to be certain as to whether the cortex was originally fully evolved or not, it is obvious that the visuo-sensory area possesses an individually deficient granule- or receptive lamina, and had commenced evolution in a manner which should have carried it beyond the level of the normal case. The latter remark applies equally to the visuo-psychic and prefrontal regions.

If, however, the cortex of this case be credited merely with evolution up to the level of the normal case, the significant fact appears that the pyramidal or psychic lamina has become decreased in depth by 24 per cent. in the prefrontal region, by 13 per cent. in the visuo-psychic zone, and by 6 per cent. in the visuo-sensory area.

MALE, AGED 44. WELL MARKED BUT NOT GROSS DEMENTIA ENCEPHALON 1280 GRAMMES. WASTING SEVERE IN FRONTO-PARIETAL AND UPPER TEMPORAL REGIONS, BUT ESPECIALLY IN PREFRONTAL; AND OF AN UNUSUALLY PURE NEURONIC TYPE. CEREBRAL VESSELS NORMAL.

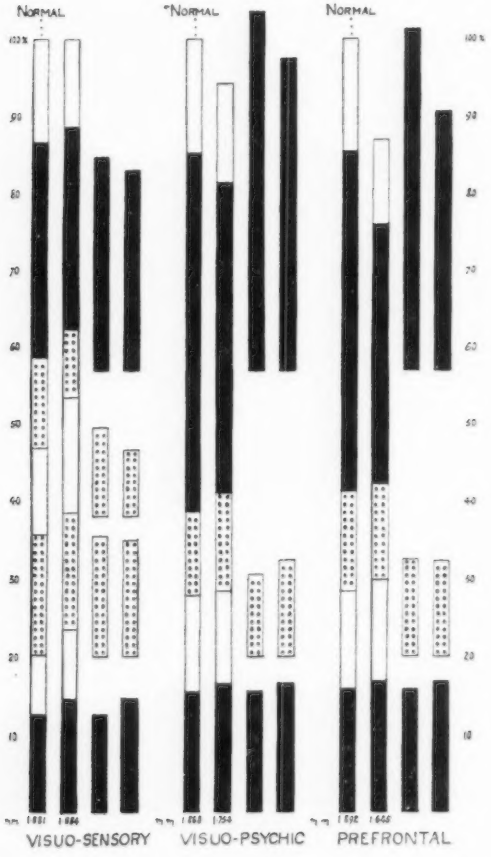

FIG. 60.

The figure shows, in comparison with the normal, the cortex of the visuo-sensory, the visuo-psychic, and the prefrontal regions of a case of well-marked dementia. From the aspect of total depth, the visuo-sensory area is normal, the visuo-psychic region shows a decrease of 6 per cent., and the prefrontal one of 13 per cent. In other words, the prefrontal region, which is the last to develop, shows the most affection, and the visuo-sensory area, which is the first to develop, shows the least. If the outer cell-lamina or pyramidal layer be considered alone, there is a decrease of 6 per cent. in the visuo-sensory area, one of 13 per cent. in the visuo-psychic zone, and one of 24 per cent. in the prefrontal region. The middle cell-lamina or granule-layer exhibits an individual decrease in the visuo-sensory area, and is very well developed in the visuo-psychic zone, and well developed in the prefrontal region. The inner cell-lamina is of a greater depth than that of the "normal" case in all the three regions, which fact suggests that the case under consideration was at any rate capable of development to a degree above that of this particular normal, even if this had not actually occurred.

Summary.—As a summary of the results of my micrometric studies, I would remark that the human cerebral cortex is originally evolved from three primary cell-laminæ; an inner or polymorphic, which is concerned with the performance of organic and non-voluntary activities; a middle or granule, which is receptive in function; and an outer or pyramidal, which serves as the physical basis of the associative or psychic functions of the cerebrum. The last of these, as has been shown by the investigations of John Turner [21] and of G. A. Watson [25], is the distinctive feature of the cortex peculiar to the mammalia, or the neopallium, to employ the term introduced by Elliot Smith.

These three laminæ appear during normal development, in the order in which I have stated them—namely, from within outwards—and the cortex of the visuo-sensory area is evolved before that of the visuo-psychic zone, and this before that of the prefrontal region.

In cases of mental disease grading from idiots and imbeciles through various types of non-demented and partially demented lunatics to the gross dement, great differences in the degree of evolution and dissolution of the cortex exist; and these, considered from the general aspect, follow the order of normal development. In amentia the condition is one of sub-evolution to different degrees, and in dementia the laminæ suffer in the reverse order to that of their evolution, the most affected being the latest developed, and the least affected being the earliest developed.

The degree and type of these differences vary according to the region of the cortex, whether this be a projection area, a zone of special association, or the prefrontal (higher associative) region.

In the case of the visuo-sensory area, the prominent features are poor evolution of the pyramidal and polymorphic laminæ and specialization of the granule or receptive lamina. There also exist individual variations in the degree of evolution of the granule or receptive lamina, and in that of the pyramidal or associative lamina, which individual variations bear no relationship to the degrees of amentia or dementia which exist in individual cases.

In the case of the visuo-psychic zone, the important feature, apart from an especially good evolution of the granule or receptive lamina, is a marked degree of individual variation with regard to the depth of the pyramidal or associative lamina. This individual variation is independent not only of the existing grade of amentia or dementia, but also of the individual variation in this lamina which occurs in the visuo-sensory area.

In the case of the prefrontal region, both specialization and individual variation are practically or entirely absent, and the cortex merely exhibits degrees of sub-evolution or dissolution which vary according to the grade of amentia or dementia which exists in the individual cases. That the condition is one of true sub-evolution is shown by the fact that the laminæ are sub-evolved in the order of their normal development, the last to appear being the least developed, and the first the most. The reverse order holds with regard to dissolution, the last lamina to appear during normal development being the first to undergo retrogression in dementia, and the first the last. In the case of the cortex of the prefrontal region, therefore, the associative function of the pyramidal lamina may be regarded as "*voluntary* associative," in view of the fact that the essential feature of amentia and dementia is decrease, instability, or loss of voluntary control over the processes of cerebral association.

As a final remark, I would add that there is reason to believe that this physical basis of the cerebral functions, which exhibits such well-marked variations in the subjects of mental alienation, exhibits equally important though less extensive variations in the case of presumably normal individuals; and thus indicates a structural origin for individual differences in mental endowment.

Chapter VII.

The Pre-Rolandic or Psychomotor Cortex.

Having completed the description of my observations and deductions with regard to the structure and functions of the visuo-sensory (or sample sensory projection), the visuo-psychic (or sample special associative), and the prefrontal (or higher voluntary associative) regions of the cortex, I now pass on to certain observations with regard to the structure and functions of the final type of cortex with which I propose to deal—namely, the pre-Rolandic or psychomotor.[1]

[1] The last number of Brain contains a paper by H. Charlton Bastian on "The Functions of the Kinæsthetic Area of the Brain." Bastian repeats his view that "the so-called 'motor-centres' are in reality sensory centres for the registration of a complex set of impressions (kinæsthetic) occasioned by movements" (p. 327); and he remarks that "it will soon be more widely recognized that there is not the slightest need for postulating the existence of 'motor' or of 'sensori-motor' centres in the cerebral cortex" (p. 340). He speaks of "a very indefinite, and to me meaningless, view suggested by some who speak of this region as containing 'psychomotor' centres. This metaphysical suggestion is neither helpful nor in any sense explanatory. It will be better, therefore, to cease to use a nomenclature which is not in harmony either with modern psychological or physiological science" (pp. 327-28).

I trust that the evidence I have produced in these lectures with regard to the structure

It is unnecessary for my purpose to describe in detail the great controversy which raged for so many years as to whether this region possessed purely motor or sensori-motor functions. I shall merely remind you of how the histological researches of Bevan Lewis and Henry Clarke, which as long ago as 1878 resulted in the delineation of the Betz-cell area, were forgotten in the heat of the controversy until 1901, when, through the experimental work of Sherrington and Grünbaum, followed by the histological researches of Campbell and of Brodmann, they finally received belated recognition.

Since that time the majority of observers have credited the precentral gyrus with motor, and the postcentral with sensory, functions; and this opinion received confirmation, so far, at any rate, as the experimental method can be regarded as capable of affording it, from the researches of Oskar Vogt [23], who in 1906 published a paper describing the results of stimulation and extirpation of the precentral and postcentral gyri. In brief, Vogt concluded that palsy without ataxy followed destruction of the precentral gyrus, and that ataxy, but no palsy, resulted from destruction of the postcentral gyrus. Last year, however, in the Linacre Lecture, Victor Horsley [15] described what he regards as a crucial test case, and reiterated his conviction that the so-called motor area is really sensori-motor. From this patient, who suffered from athetoid movements of the left hand, followed by violent convulsive movements of the whole upper limb, Horsley removed by operation the portion of pre-Rolandic cortex which, as the result of stimulation, he concluded to constitute the whole of the arm area. He carefully describes the immediate results which were partly motor and partly sensory, and the remote results (a year later), which consisted of permanent absence of spasmodic movements, partial recovery of voluntary movement of the left upper limb, and considerable recovery from the sensory disability. On this case Horsley bases his contention that the precentral gyrus is sensori-motor in function.

The evidence which I purpose laying before you points to very different conclusions regarding the functions of this region of the cortex, and, unless these conclusions are correct, the whole of my

and functions of the "psychomotor" area will be sufficient to absolve me from the reproach contained in the last quotation.

I am responsible for coining the terms "visuo-sensory" and visuo-psychic," which latter seems to me preferable to "visual cerebral-associative"; and these terms have been generally adopted and have been extended by Campbell and others to the auditory, &c., areas. The term "psychomotor," employed by me in preference to the cumbrous "cerebral-associative motor," seems equally satisfactory. I hope to be pardoned for failing to see in it any "metaphysical suggestion."

previous observations and deductions fall to the ground. I would therefore submit that in my opinion the experimental method, even in the hands of so renowned an operator as Horsley, cannot be regarded as trustworthy. On purely theoretical grounds, it might well be doubted whether a gyrus of considerable size could be removed without any disturbance of the functions of the immediately adjacent gyrus resulting, but in this instance anatomical reasons exist which appear to me to render such an operation a practical impossibility. To indicate these I will now show (fig. 61) naked-eye sections through the fissure of Rolando, which are situated above and below the buttress and thus indicate the arrangement of the neighbouring gyri in both these positions. I introduce the two sections in order to avoid the possible

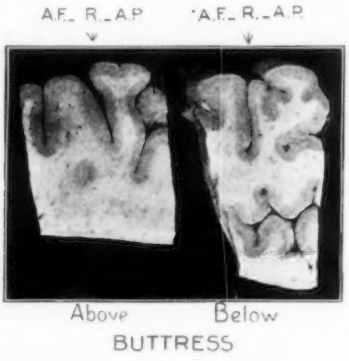

FIG. 61.

Naked-eye sections across the central convolutions. The left-hand section is above the buttress, and the right-hand section is below this annectant. R., furrow of Rolando; A.F., precentral or ascending frontal gyrus; A.P., postcentral or ascending parietal gyrus. Both sections show the extremely narrow neck of the postcentral gyrus, and the right-hand one also indicates the proximity of the gyri of the parietal operculum. The figure demonstrates that removal by operation of the precentral gyrus, however skilfully performed, must necessarily result in functional, and probably also in structural, damage to the fibres entering the neck of the postcentral gyrus.

criticism that the arm area is not included, since this area was placed above the buttress as the result of the earlier stimulation experiments on man, although it is now considered to lie below this annectant.

In the first section, which is above the buttress, is seen the extremely narrow neck of the gyrus postcentralis, and the nearness of this to the site of operation.

In the next section, which is below the buttress, the same point is

equally clearly visible, as is also the relative nearness of the gyri of the parietal operculum to the seat of operation.

Apart entirely from the intimate structural and functional associations of the pre- and postcentral gyri, these photographs in my opinion indicate the probability, I may even say the certainty, that removal of the precentral gyrus, however carefully performed, will result in functional, if not also in actual structural, disability of the fibres passing to and from the postcentral gyrus.

I now pass on to the consideration of the structure of the precentral gyrus, from the aspect of cell lamination. In the case of this region I have not resorted to the micrometric method, partly because the structural conditions preclude the possibility of obtaining a series of measurements from the four situations I am accustomed to select, and partly because the practical absence of a middle cell-lamina or granule-layer renders measurement of this lamina untrustworthy even if possible. I therefore propose to illustrate my point, not by series of measurements from human subjects, but by exhibiting certain mammalian cortices which show the depths of the various laminæ in a cruder but equally satisfactory manner. As a preliminary remark I would state that the lamination of the precentral gyrus, though to the inexperienced eye indefinite, is of the usual general type, consisting of an *outer fibre-* or superficial *lamina*, an *outer cell-* or pyramidal *lamina*, a *middle cell-* or granule-*lamina*, an *inner fibre-lamina* or inner line of Baillarger, which here contains the Betz cells, and an *inner cell-* or polymorphic *lamina*.

The photographs which form the following figures are strictly comparable, apart from the somewhat lower magnification of fig. 64.

The following plate (fig. 62) is taken from the Betz-cell region of the dog. It shows all the five laminæ—namely, the superficial, the pyramidal, the indefinite granule, the inner line of Baillarger with Betz cells, and the polymorphic lamina.

I wish particularly to draw your attention to the fact that the second lamina or pyramidal layer (·45 mm.) is in depth about one-third of the combined depth of the laminæ below it (1·18 mm.) I would also point out the large size and generally embryonic condition of the cells in all the laminæ.

The next photograph (fig. 63) illustrates the precental cortex of the rhesus, with its five laminæ.

I would particularly ask you to note that the depth of the pyramidal lamina (·91 mm.) is practically equal to the conjoined depth of the laminæ below it (·90 mm.), and also that the individual cells of all the

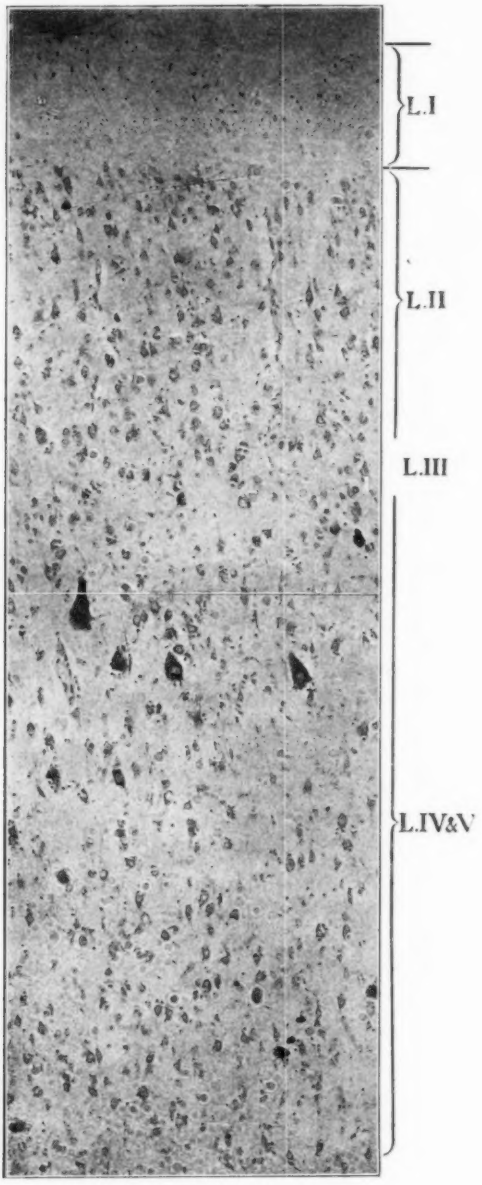

FIG. 62.

Eighty-nine diameters. Cortex of the Betz-cell area of the dog. L.I, outer fibre- or superficial lamina; L.II, outer cell- or pyramidal lamina; L.III, the indistinct middle cell- or granule-lamina; L.IV and V, the inner fibre-lamina, or inner line of Baillarger containing Betz cells, and the inner cell- or polymorphic lamina. The depth of L II is about one-third of the conjoined depths of L.III to L.V. The cells are of large size, and are embryonic in appearance.

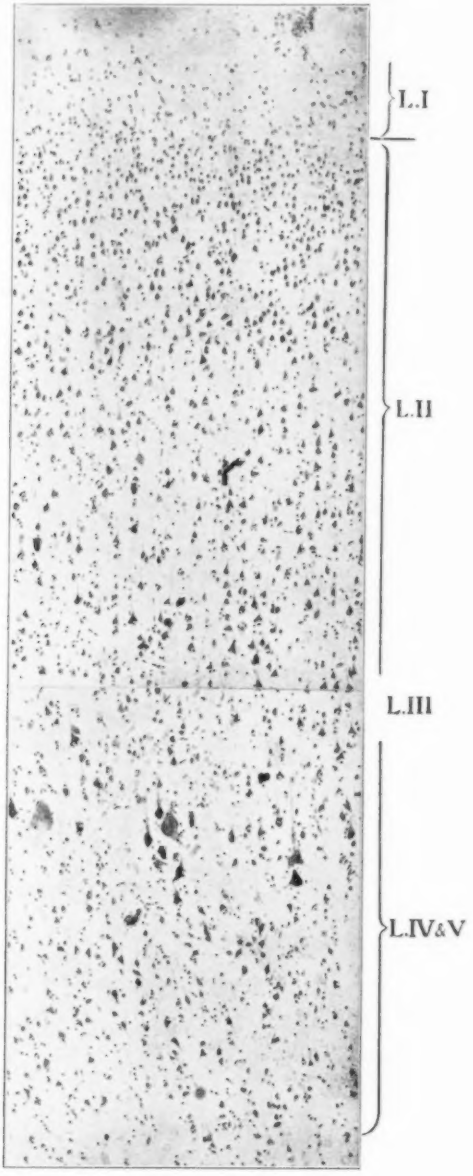

FIG. 63.

Eighty-nine diameters. Cortex of the Betz-cell area of the rhesus. L.I to L.V as in the preceding figure. The depth of L.II is practically equal to the conjoined depths of L.III to L.V. The constituent cells are smaller and more numerous than in the dog, and are also better made and relatively further apart.

laminæ are smaller and more numerous than in the dog, and are also better made, and relatively more widely separated from one another.

The next photograph (fig. 64), less highly magnified, shows the cortex of the human precentral gyrus, with its five laminæ.

I would draw your attention to the fact that the second or pyramidal lamina (1·24 mm.) is in depth four-thirds of the conjoined depth of the laminæ below it (·92 mm.), and also to the detail that the individual cells are very well made, and are more widely separated from one another than in the rhesus.

A study of these cortices leads to the following conclusions:—

The outer cell-lamina or pyramidal layer of the dog is one-half of the depth of that of the rhesus, which again is three-fourths of that of the human subject.

The middle cell-lamina is so deficient in depth as to be practically invisible, except to the experienced observer.

The conjoined depth of the lower laminæ is practically the same in the rhesus and man, and is one-fourth deeper in the dog than in the others.

The ratio of the depth of the second or pyramidal lamina to that of the three lower laminæ is in the dog about one-third, in the rhesus 1 1, and in man 4/3. In man, therefore, the precentral ratio is as high as or slightly higher than in the prefrontal region, in which general average measurements give an average ratio of about 11/10.

As a very rough analogy, the pyramidal lamina of the dog may be compared with that of a stillborn infant; and the pyramidal lamina of the rhesus with that of an imbecile.

Finally, in passing from the dog to the rhesus, and from the rhesus to man, there is a very marked and progressive improvement in the development of the individual cells in all the laminæ, which general improvement, however, pales before the great difference which exists in the three cortices with regard to the evolution, both in depth and in content, of the outer cell- or pyramidal lamina.

In view of the conclusions which I expressed in the last chapter with regard to the functions of the primary cell-laminæ of the cortex, the deduction is evident.

The outer cell- or pyramidal lamina, which is of psychic, associative, and educative significance, is the prominent feature of the precentral cortex of man.

The granule- or receptive lamina is reduced to a minimum depth in

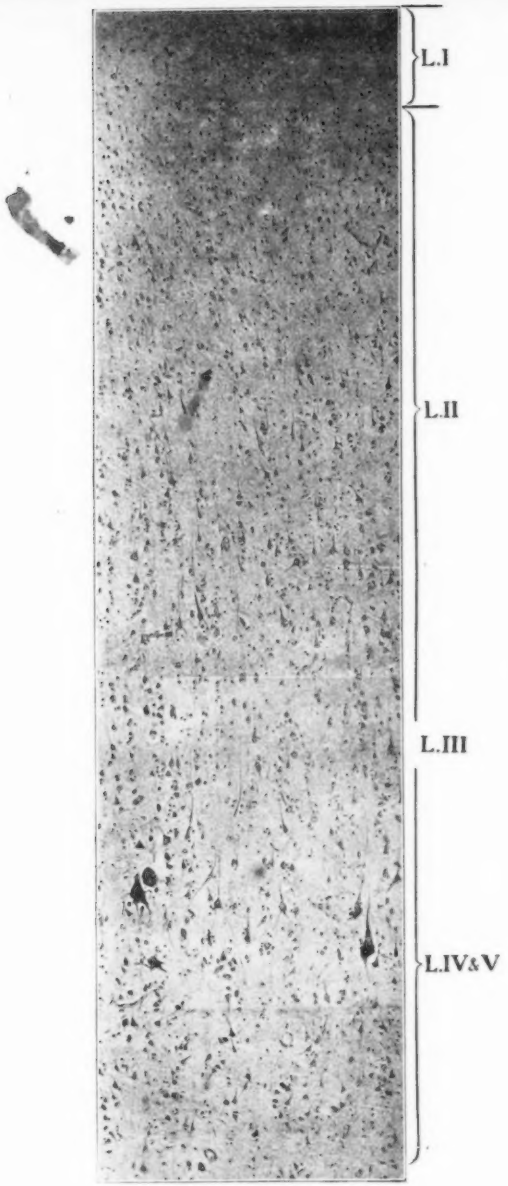

FIG. 64.

Seventy-four diameters. Cortex of the Betz-cell area of man. The magnification is five-sixths of that of figs. 62 and 63. L.I to L.V, as in the preceding figures; L.II in depth $\frac{4}{5}$ of the conjoined depths of L.III to L.V. The constituent cells are very well made, and are further apart than in the rhesus. A comparison of figs. 62 to 64 shows that the essential differences between the cortices consist in a very marked and progressive improvement in the development of the individual cells in all the laminæ, and, particularly, in the degree of evolution of L.II, the pyramidal lamina, of the several cases. L.II, the outer cell- or pyramidal lamina, which is of psychic, associative, and educative significance, is thus the prominent feature of the precentral cortex of man. L.III, the granule- or receptive lamina, is reduced to a minimal depth in all the cortices. L.IV and L.V, which are of organic and instinctive significance, are similar in type in man and the rhesus, and in the dog their depth is somewhat greater, and their constituent cells are more embryonic in structure.

all the cortices. This fact negatives the possibility of the existence of sensory-receptive functions in this part of the cortex.

The fourth and fifth laminæ, which are of organic and instinctive significance, are of the same depth and general type in man and in the rhesus, and in the dog their conjoined depth is one-fourth greater and their individual cells are more embryonic in structure.

The obvious conclusion, therefore, is that in man the psychic, associative, and educative functions of the precentral gyrus are paramount; that in all three the receptive functions are minimal or non-existent; and that the organic and instinctive activities are approximately on the same level in all the three.

When this conclusion is regarded in association with the well-known truth that the particular type of cortex under consideration increases in area and differentiation during the ascent of the mammalian scale, not according to muscular bulk but according to the degree of motor educability exhibited by the several parts of the body, the further conclusion that the Betz cells merely serve as a relatively simple motor mechanism, and that motor educability must have its seat in the second or pyramidal lamina, is inevitable. That the Betz cells serve as the origin of the pyramidal tracts has long been believed. It is, in fact, many years now since I noticed well-developed Betz cells in the cortex of a fœtus of six months, and therefore took for granted that they served as the origin of these tracts. The truth of this presumption has recently been finally proved by Holmes and Page-May [14]. Further, it has long been known to physiologists that whilst the pyramidal tracts normally conduct voluntary efferent impulses, such impulses in the functional absence of these tracts can still find passage. For example, a hemisection of the spinal cord of a dog, followed by a higher hemisection on the opposite side, and this again followed by a still higher hemisection — this time on the original side — results in at least a very considerable return of power over both lower limbs.

It may thus be regarded as proved that the Betz cells serve not as the psychomotor cortical mechanism, but simply as a subservient mechanism for the direct transmission of voluntary impulses to the lower motor centres.

I may add, as a necessary consequence to this conclusion, that the Betz-cell distribution need no longer, therefore, be regarded as indicative of the limits of the cortical zone concerned with the evolution of those associational processes which, when translated by the agency of the lower motor centres into muscular movements, constitute the sole

objective indications of cerebral activity. If, as I consider proved, reliance can be placed on the results of the histological investigations of the past decade, the educable psychomotor cortex, with little modification, extends over almost or quite the posterior half of the frontal lobe, where it grades, through cortex of an intermediate type, into that of the prefrontal region.

Having, as I hope, sufficiently indicated my reasons for regarding the precentral cortical zone as psychomotor, rather than motor or sensori-motor, in function, I will now exhibit as a histological contrast a plate prepared from an illustration (fig. 65) published by Gordon Holmes [13], in order to show the well-defined middle cell-lamina or granule-layer which exists in the postcentral gyrus. The proportion which the depth of this lamina bears to the total depth of the cortex—namely, about one-eighth—is, to me at any rate, sufficient almost to prove that this cortex belongs to a sensory-projection sphere; in other words, to indicate with great probability the performance of sensory-receptive functions by the postcentral gyrus.

Chapter VIII.

Provisional Scheme of the Localization of Cerebral Function.

The general trend of the results of the recent histological survey of the cerebral cortex, which followed the enunciation by Flechsig of his doctrine of centres of projection and centres of association, and which has culminated in the elaborately detailed descriptions of Brodmann, has, to say the least, been highly suggestive of the existence of a definite correlation between histological structure and functional significance: and it is probable that the histological method, without entirely replacing the experimental, will in the future be still more fruitful in this direction. In the personal investigations which I have described I have endeavoured by the employment of subnormal and pathological material to obtain proof of the functional significance of certain of the histologically differentiated regions of the cortex. Such proof as I have obtained leads me to adopt, as a partially proved provisional hypothesis, the following scheme of the localization of cerebral function. I do not claim originality, except with regard to the production of proof of functional significance, since in dealing with cerebral function one needs to select rather than to enunciate opinions, owing to their multitude.

I would regard the human cerebrum, not as a sensori-motor, but as an intermediate or associative ganglion, which, on the one hand, receives

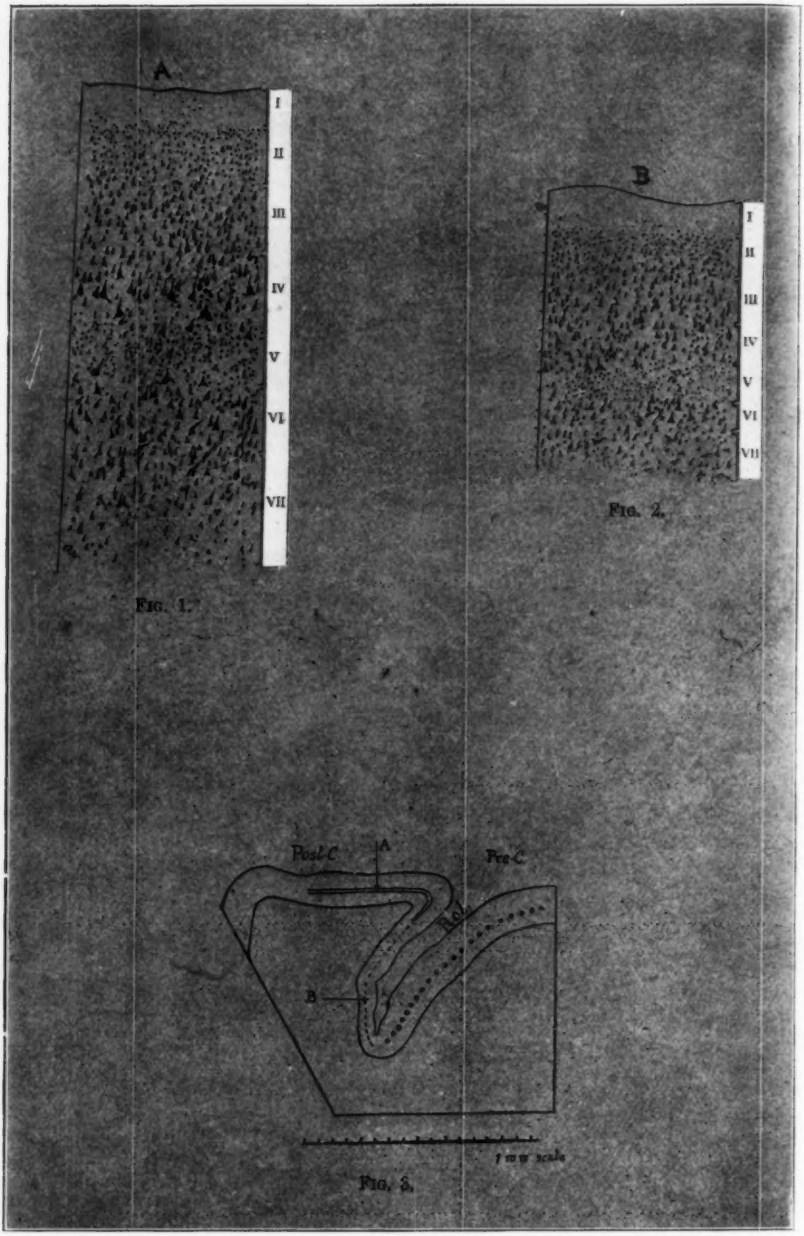

FIG. 1.

FIG. 2.

FIG. 3.

FIG. 65.

(Gordon Holmes.) In A and B respectively is shown the structure of the cortex of the postcentral gyrus at the regions indicated in the lower diagram. I = L.I, the outer fibre- or superficial lamina; II to IV = L.II, the outer cell- or pyramidal lamina; V = L.III, the middle cell- or granule-lamina. VI and VII indicate respectively L.IV, the inner fibre-lamina, and L.V, the inner cell- or polymorphic lamina. The possession of such a well-developed granule-lamina (V = L.III) by the postcentral gyrus markedly contrasts with the almost complete absence of this lamina in the precentral gyrus. The performance of sensory-receptive functions by the former gyrus is therefore highly probable.

sensorial impressions and elaborates them, by processes of association, into the physical equivalents of psychic products of high complexity, and which, on the other hand, to a variable extent controls, selects, and co-ordinates certain of these equivalents, eventually transforming them into further physical complexes, whose function is to set in action the lower motor centres. On this functional basis I would divide the cerebrum into pre- and post-Rolandic portions, the former of which possesses controlling and executive functions, and the latter receptive and elaboratory.

I would subdivide the pre-Rolandic part, or frontal lobe, into a posterior or psychomotor area which is concerned with the evolution of such physical complexes as are necessary to give external expression to the results of cerebral association; and into an anterior or prefrontal area which is able to control, select and co-ordinate certain of the results of post-Rolandic cerebral association, and either to allow these to undergo psychomotor transformation or to inhibit this process. Both these functions I regard as proved, and I consider the outer cell or pyramidal lamina of the cortex to be at least the chief seat of their actual performance.

The cortex of the post-Rolandic portion of the cerebrum I would regard as consisting of projection areas, of which the visuo-sensory area is a type. Each of these is surrounded by, or possesses in its proximity, zones of special association, of which the visuo-psychic region is an example, which zones are hall-marked in function according to their appropriate projection areas. It also consists of intermediate cortex, in which are fused and elaborated the results of the special processes of association. I consider the functions of the visuo-sensory and visuo-psychic regions of the cortex to be proved, and, from homology, the functions of the other areas of projection and special association, the exact location of which is still probable rather than certain. I regard the outer cell- or pyramidal lamina as at least the chief physical basis of these processes of association, and the middle cell- or granule-lamina of the projection areas as the region concerned with the reception and immediate transformation of sensorial impressions. I may, perhaps, here remind you that the middle cell- or granule-lamina attains to its maximum degree of development in the sensory-projection areas, and that it continues to be well developed in the special zones of association. In both these types of cortex there is no clear line of demarcation from the laminæ above and below it. The granule-lamina is of good development in the posterior region of general association, and also in the prefrontal area, in which latter it is more distinctly separated from the

laminæ above and below it than in any region with which I am familiar. From the prefrontal region backwards, the granule-lamina decreases in depth and distinctness until, in the psychomotor area, it reaches a minimal depth and is barely discernible.

The inner cell- or polymorphic lamina, as I have already stated, has been shown to be the prominent lamina in the lower mammalia, and must be regarded as subserving such organic and instinctive activities as are not acquired by education. It is probable, for reasons which I have indicated, that this is its function in man.

Chapter IX.

The Nature of Language and the Language Mechanism.

For the further consideration of this scheme of cerebral function, and, in particular, in order to indicate the probable nature of the cerebral processes which subserve the exhibition of certain of the more important symptoms of mental disease which do not fall under the gross generalization of amentia and dementia, it is necessary that I should now introduce a few observations with regard to the nature of language.

Owing to the complexity of even the more elementary processes of cerebral association, a mechanism for the symbolic representation of the results of these processes soon becomes a necessity. The mathematician, for example, has evolved a complex system of symbols in order that he may be able to perform complicated operations with masses of figures elaborated from the ten numerals alone. He thus unconsciously imitates the infinitely more complex system which has been elaborated in association with the higher evolution of the cerebral functions—namely, the language mechanism—whose "numerals," or sensori-memorial images and crude sensations, are innumerable.

Words, or language symbols, are of very different representative value. Articles, pronouns, prepositions, conjunctions, interjections, and the simpler adjectives, adverbs, and verbs, when thought of alone, as a rule arouse little beyond their respective visual or auditory word-images, which in themselves are meaningless.

Adjectives, adverbs, verbs, and abstract nouns, when thought of alone, arouse first their respective visual or auditory word-images. These, however, are meaningless until by complex processes of association they are defined and illustrated through the sensori-memorial spheres attached to the various sensory or projection areas.

Common or proper nouns, when thought of alone, may first arouse their visual or auditory word-images; but they frequently at once awaken a whole series of processes of association, and thereby determine the reproduction of sensori-memorial images attached to one or more of the several sensory or projection areas. I may remark that each of such series of processes of association differs in detail on each occasion on which it is evolved. For example, the mental processes induced by the word "microscope" are different, not fundamentally but in detail on each occasion on which they are aroused. This ever-varying perceptive content is consequent on the revivification of, and the modification of the complex relations of, the numerous existing sensori-memorial images of which the word is symbolic, which are constantly taking place under the influence of even apparently unrelated afferent impressions.

Perception, therefore, is a cerebral process which is similar in nature, but differs in detail, on each occasion on which it occurs. It is thus incorrect to speak of a cerebral centre for percepts, which are psychic products that, except by accident, need never be identical even if the arousing sensation is the same. I may remark that perception can hardly be described as the act of naming objects, for it is as often the reverse—namely, the act of applying one or more sensori-memorial images to a name, or the identifying of a sensation with a sensori-memorial image. The last corresponds to the crude perceptions of animals; the others to perceptions involving the employment of the symbolic mechanism of language.

Similarly, the process of conception may take the form either of generalization from a series of sensori-memorial images to a general name, or of revivification of a series of sensori-memorial images in order that the meaning of a general name may be interpreted. This process is invariably a very complex one, and necessarily differs in detail, in spite of a general similarity in nature, on each occasion on which it occurs. It is thus incorrect to speak of a cerebral centre for concepts.

Language is produced by the suitable co-ordination of words of different symbolic value; and by its means alone is it possible to perform the highly intricate processes of cerebral association which form the physical bases of judgment and reasoning.

Words are, from the afferent aspect, mere sensations, the memories of which are stored in the appropriate zones of association attached to the particular cortical projection areas to which they happen to pass. For example, a word seen stimulates the visuo-sensory area, and the resulting image is stored in the neighbouring visuo-psychic region.

On the other hand, from the efferent aspect, words are mere articulatory or cheiro-graphic results of the action of complex neurone groupings in the outer cell- or pyramidal lamina of the psychomotor area. This fact may be illustrated by the common observation that children learning to write contort their faces and tongues during their endeavours to perform the necessary manual operations.

In the complete mechanism of language, words thus possess, from the afferent aspect, four sensori-memorial bases in the cortex—namely, in the neighbourhood of the auditory and visual projection areas of the cortex, and in that of the kinæsthetic projection area lying behind the fissure of Rolando, in especial relation to those portions concerned with the reception of sensations from the larynx and the hand.

From the efferent aspect, words possess two motor-memorial bases in the neighbourhood of those parts of the psychomotor area lying in front of the fissure of Rolando, which have been shown both experimentally and histologically to be concerned with the evolution of acquired movements of the larynx and the hand.

Words are originally acquired and reproduced through imitation by means of the auditory and articulatory word-centres, the latter working in conjunction with its sensory coadjutor, the articulatory-kinæsthetic word-centre.

In the evolution of the mechanism of language, suitable and highly complex associations occur between these various word-centres. These associations are of such a nature that the language machine can, and frequently does, act as a mere mechanism for the evolution and reproduction of language which to the individual may be meaningless.

For example, children when learning to speak are often obviously ignorant of the meaning of the phrases they employ; and when older learn a large portion of their lessons by rote and frequently but feebly appreciate their meaning. Adults can learn the Lord's Prayer backwards, or sentences in an unknown foreign tongue; and uneducated persons are often fond of using, and quite wrongly using, words which take their fancy and the real meaning of which they do not in the least understand. Imbeciles can sometimes learn by rote long paragraphs of the meaning of which they are ignorant. Lunatics often employ the language machine in an almost entirely mechanical manner.

Examples of this mode of employment of the language mechanism may be readily drawn from everyday life. Many word-complexes which are frequently repeated—e.g., daily prayers—are often gone through in a purely mechanical manner, whilst the individual reproducing them is

perhaps, thinking of something else. Again, it is appreciated by few that language, as normally employed, is very largely a purely reflex, or, at any rate, automatic function, and that the significance of what is spoken is but feebly appreciated by the speaker. This is particularly evident in the case of persons who talk without having anything particular to say, and who bore every listener they meet with the same personal experiences, the same stale stories, and the same gossip.

By these few remarks I have endeavoured to indicate and illustrate the fact that words are merely symbols which possess different grades of value, and which are meaningless unless they are employed to incite the occurrence of such processes of cerebral association as are necessary to awaken the various sensori-memorial images of which such words are but the symbols. In order, therefore, that language may possess meaning, there necessarily occurs, during the employment of its mechanism, an active associational participation on the part of practically the whole mantle of the cerebrum.

As a preliminary to the consideration of the manner in which the language mechanism is voluntarily employed, I would remark that words, in my opinion, invariably arise into consciousness through the activity of sensory spheres, and may do so through that of any one of them. When, however, they are voluntarily and silently reproduced—i.e., thought of—words are invariably awakened through the articulatory-motor word-centre under normal conditions. Further, this reproduction requires a muscular effort, and cannot take place without a definite attempt at articulation, usually, but not necessarily, accompanied by a slight expiration. Again, words cannot be voluntarily repeated in thought by means of the cheiro-graphic centre if the hand is not actually moved, unless such hand-movements are replaced by slight movements of the head, or even of the lower jaw or the eyes, through the agency of their respective motor spheres. Such observations as I have just indicated are valuable because they render it probable, if not certain, that the important factors in the reproduction are not the muscular movements but the sensory impulses derived from them; otherwise there is no reason why such muscular movements should not be imagined, without any attempt at their actual performance. I thus consider that words, when voluntarily reproduced, are invariably awakened through the preliminary action of the prefrontal region on the psychomotor area, activity of which results in stimulation of appropriate neurone complexes subserving the evocation of the particular sensori-memorial images, which arise in the zone of special association attached to one or more of

the sensory projection spheres. This view, I may remark, is merely an elaboration of that long ago advanced by Hughlings Jackson, more recently supported by Stricker, and strongly combated by Bastian [1].

Whether the rousing of such sensori-memorial images is followed by further processes of cerebral association, and what these further processes are, if they occur, depends partly on the general condition, as regards excitability, of the lower centres of association and partly on such degree of voluntary guidance and control of these processes as happens to be exercised. For example, in dreamy states, when voluntary selection, co-ordination, and control are at a low ebb, processes of lower association, involving the awakening of all kinds of sensori-memorial images, occur in a more or less riotous manner according to certain general laws which are well known and need not be further referred to here. On the other hand, as an extreme example, during the voluntary employment of written or spoken language for the evolution and reproduction of the higher psychic products—e.g., the production of an abstruse thesis—voluntary control over, and guidance of, the processes of lower association is paramount. In such a case, however, there is a tendency, which requires to be continually combated, for the cerebral processes to keep to the general lines of the mechanism of language, to the exclusion of such processes as involve the evocation of visual sensori-memorial images of the ordinary type. In other words, during the voluntary employment of written or spoken language for the evolution and reproduction of abstract thought, there is a tendency for the performer to become unintelligible to others, and perhaps even to himself, unless he continually reverts to concrete examples.

Chapter X.

Defective Control of Processes of Lower Association in Mental Disease.

In the insane—as I shall now illustrate by examples—voluntary control over the processes of lower cerebral association, including the activity of the language mechanism, is to a greater or a lesser extent defective.

In amentia, according to its grade, such voluntary control is permanently or temporarily defective. In many of the lowest types the mammalian tendency to sleep, unless the processes of lower association are stimulated by sensory or organic stimuli, is observable. On the other hand, in attacks of simple mania occurring in the higher grades

of amentia, the prefrontal centre of higher control is in functional abeyance and the cerebrum acts as an uncontrolled sensori-psychomotor machine. Instead of — as normally happens — but a small selected number of the ever-entering stream of afferent impressions being noticed, almost every visual and auditory stimulus which arrives at the cortex is accepted. Processes of cerebral association incited by these occur pell-mell, and find motor expression in emotional disturbance, rapid movements, and a riotous display of words. It is impossible to obtain more than the momentary attention of the sufferer. This condition of uncontrolled sensori-psychomotor activity may last for hours, days, or weeks, after which the patient becomes—at any rate for the time—sane.

Again, in dementia, according to its grade, voluntary control over the cerebral processes of lower association is permanently defective or absent. If this be defective, and the centres of lower association be normal, the chief clinical features exhibited by the patient are a general hebetude and a lack of interest in his surroundings. If, however, aberrant states of the centres of lower association exist, certain additional symptoms, to which I shall refer later, are presented. Further, in the grosser grades of simple dementia, no evidence whatever of the existence of cerebral activity may be exhibited or obtainable, and the patient is an inanimate object, unable even to feed himself or to attend to the calls of nature.

I will mention as a final example the numerous cases of premature dementia which exhibit strange motor phenomena, and which are commonly classed under the term "catatonia." I believe that these phenomena are due to the occurrence of a more or less extensive dissolution of the neurones of the psychomotor area in certain subjects, usually juvenile, in whom the fundamental psychomotor neurone-groupings are still imperfectly organized into relatively stable complexes. The pathological condition is thus, on the one hand, one of sub-evolution of function, and, on the other, one of dissolution or involution, the tract of cortex involved being practically the whole frontal lobe.

Such motor phenomena resemble, in brief, those which would occur in a "Frankenstein-man" or "mechanical model," in which certain parts were imperfectly fashioned; in which certain groupings of parts were imperfectly tested and not in proper running order; in which the higher mechanical complexes were imperfectly controlled and co-ordinated into series, and, therefore, tended to stop, to repeat action, or to go by fits and starts; and in which, owing largely to the existence of several sources of motive power (i.e., from the different organs of sensation), certain

mechanical complexes tended to run independently in consequence of an imperfect general co-ordination of, and control over, the whole mechanism. The motor phenomena are thus varied, and are, on the whole, of a distinctly positive or a definitely negative nature: and repetition, wayward and grotesque action, &c., are common.

In chronic cases the phenomena are often still further complicated as regards an immediate explanation, but simplified as regards their actual exhibition, by a more or less extensive dissolution of neurones, which results in stereotyped motor remainders of former skilled accomplishments. These, occurring on the dissolution side of the scale, differ in character from the erratic, grotesque, repeated, mechanical-model-like, and often unskilled movements which occur on the sub-evolution side and are due to imperfect control and insufficient practice.

That this explanation is probably correct is indicated by the fact that in a series of chronic cases of premature dementia without motor phenomena, 55 per cent. exhibited a moderate grade of dementia, whereas in a series presenting motor phenomena as many as 73 per cent. had attained a moderate grade of dementia. I may remark that this grade of dementia indicates the existence of intracranial morbid appearances of moderate intensity, these representing the usual final stage which cerebral dissolution reaches in the absence of marked degeneration of the cerebral arteries.

Chapter XI.

Independent Activity of the Centres of Lower Association. Illusion and Hallucination.

I now pass to the consideration of certain phenomena due to the independent activity of the centres of lower association. Words, when voluntarily reproduced in thought, are awakened through the action of the prefrontal cortex on the psychomotor area, this commonly being followed by activity of one or more centres of special lower association, and often by that of the whole region of general lower association. Such are therefore regarded as normal products of thought of *personal* origin. The other normal, and in this case non-personal, mode of origin, which applies to all types of sensation, is of course that of sensory stimulation.

A third mode of origin of words, and also of other varieties of sensori-memorial image, is, however, common in normal persons; and if the mode is not more common, the results of it are at any rate more

obtrusive in the subjects of mental disease. I refer to the spontaneous arising of words or other sensori-memorial images in the auditory or visual centres of lower association. From my experience of these phenomena in the subjects of mental disease, I have no hesitation in classing all such as hallucinations, which hallucinations may or may not be distinguished by the subject from true auditory or visual sensations. A homologous phenomenon to such a hallucination may be observed during the stimulation of the psychomotor area of a monkey which has recovered from anæsthesia. Such an animal regards the movement, say, of the arm with great surprise, and at once performs a voluntary and opposite movement, exactly as if the limb had been moved by an external agency. The resemblance between this response and the behaviour of a lunatic who is replying to "voices" is striking.

In the normal wide-awake condition such phenomena are, I believe, commonly discounted as memories or illusions; and when they occur during partial sleep or dreamy states and during sleep, the term "dream" is regarded as a sufficient explanation. In dreamy states these phenomena are very common, and are as a rule largely of a visual nature. In such, in my own case, whilst all kinds of complicated experiences occur in which I appear to take part, I have usually a more or less definite consciousness of personal aloofness from the phenomena, although, however impossible, they appear quite real. During sleep, on the other hand, this consciousness of personal non-participation is not present, and the phenomena, whether visual or auditory, whilst as a rule they are based on recent experience, often derive more of their content from the past. A very common experience of mine during the recent general election, when graphic representations of the state of parties appeared in the papers, was based on a combination of these illustrations and of my illustrations of cortical measurements. I seemed continually to be discovering that my measurements did not agree with my clinical cases, or that I had made mistakes in my deductions, only to find on awakening that I had been discovering columns indicating the state of the parties in my tables, or erroneously comparing such columns with my cases.

In some instances psychomotor activity ensues, and such persons may hear a reply to responses made to their remarks, and may even keep up a short conversation, of which they know nothing when they awake. Again, in the case of some persons, including myself, the first word or two spoken by the subject awaken him, and he remembers vividly what he has said and also the remainder of the phrase he was about to

reproduce. On the other hand, many lunatics will talk to themselves, and reply to voices, for long periods of time, until their attention is attracted, after which they may revert to the former state of non-voluntary or semi-voluntary sensori-psychomotor activity.

Whilst most sane people interpret all such phenomena as "dreams," many instances nevertheless occur in which the subject, though otherwise sane, regards them as actual experiences of another world and strongly denies that he has merely been asleep and dreaming. In such cases credulity appears to be followed by belief, in a similar manner to that in which expectation results in increased sensitiveness to external impressions and often in the experience of illusions.

All these phenomena I regard as the homologues of, and as thus affording the explanation of, the more marked phenomena which are exhibited by the insane. Since such phenomena are in practice at times difficult to distinguish from, and in fact are often associated with, illusions, I shall refer to these before proceeding to remark on the subject of hallucination in the insane.

Illusions are common in sane individuals, and develop after a sensory stimulus which is of sudden occurrence and also either of short duration or of low intensity, especially when this stimulus is applied to a recognitive field which is in a hyper-excitable or expectant condition.

An example of the former is the sudden meeting, in a crowded street and under conditions which preclude a second and confirmatory sensory stimulus, of someone closely resembling a known individual. After such an experience, either doubt or certainty as to the correctness of the recognition may exist, although the individual seen may really have been a stranger; and in this case at least an illusion has been experienced.

The commonly cited example of the latter mode of development of an illusion is the recognition, in a faint illumination, of a window-blind or a white object as a ghost, which false recognition is, as a rule, readily corrected by further examination of the source of the sensory stimulus. It is perhaps, however, more common to meet with illusions of this type in the case of auditory stimuli, as when unexpected sounds are heard at night, or when certain expected footsteps or other sounds are being intently listened for. Such illusions are, as a rule, temporary. They cease if an increasing or a fading away of the auditory stimulus leads to the rejection of the false recognition; but they may persist if a fading away of the auditory stimulus occurs in association with a highly expectant condition of the recognitive field, and in the absence of additional and corrective visual or other sensory stimuli.

Illusions in the insane are similar in their psychic characteristics to those in the sane, but are more common, and on the whole are more likely to be accepted as true. This is especially the case when they occur in patients suffering from mental confusion or from dementia, for reasons which time does not permit me to dilate on.

A similar remark applies to hallucinations when occurring in the insane. It may in fact be stated that, considered generally, cases of amentia respond to illusions and hallucinations as do sane individuals, whereas cases of mental confusion or of dementia accept these as true without examination.

For instance, in certain examples of recurrent insanity these psychic phenomena do not suggest objective reality to the sufferer, who can, according to his degree of intelligence and his command of language, describe their characters and their modes of origin. As an illustration, I will cite the following remarks: "I thought my earthly father appeared in a flash under the fire-escape at the front. A man I was working with went under it and like as if he appeared to me in that man. That's where the idea sprang from." . . . "I hear my father's spirit at night, my earthly father's, guiding me, not like a voice but a spirit; whether it's a memory of his voice I don't know, like what I've heard him saying, sayings of his, and he tells me to believe in a God above, a Supreme above, and that he's in heaven, so it 'uld be a good job for me so long as he is safe in heaven—let me be safe, you know."

Again, a patient in a letter to me remarked: "I object to my muttered thoughts being known. I object to people being employed to pour nonsense into my ears. This treatment has a bad effect upon my nerves. It results in my muttered thoughts not invariably reflecting my views, desires, and intentions."

As a further instance, I will cite the following remarks of a man who was actively suicidal: "Evil thoughts overwhelm me which are wrong to God and me, evil thoughts about God even, which I don't believe in, as if an evil spirit was in me flashing an evil thought, if you understand what I mean. These thoughts have now, for the time being, become almost a part of myself, if you understand, and I feel the longer I am alive the greater is the punishment within myself, and the punishment in the future will be greater." From this description it would appear that the patient is gradually becoming more and more desperate owing to the activity of certain parts of his auditory zone of association, which spontaneously generates these particular verbal groupings he describes as thoughts.

In other examples of amentia, and especially in individuals who have little capacity for or habit of thinking, these phenomena possess a more or less objective reality, although by suitable interrogation it is, as a rule, easy to determine that the "voices" or experiences differ considerably in character from the normal products of the recognition of sensory stimuli. This difference is also evident from a consideration of the observation that the sufferers usually endeavour to determine the source of the phenomena, and, in their inability to do this, refer them to agencies of the action of which they are ignorant,—e.g., X-rays, telephones, cinematographs, &c.

On the other hand, in certain cases of mental confusion,—e.g., alcoholic confusion with marked tremor, which leads to aberrant visual stimuli, or confusion occurring in association with blocking of the external auditory meatus, or with disease or disorder of the middle ear, either of which may lead to the occurrence of aberrant auditory stimuli—the psychic phenomena are very largely caused by these aberrant sensory stimuli, although it is probable that in at any rate a large number of cases a definite part is played by deficiency or aberration of the processes of reproduction of associated memories under the influence of different aberrant sensory stimuli. Further, in many cases the sensory stimulus is probably relatively or entirely normal, but illusions result in consequence of certain associated memories, out of the enormous number of psychic units which may possibly be revived under the influence of external stimuli, being exceptionally liable to recrudescence. Whilst any of these psychic phenomena come under the definition of illusion, those of the latter type gradually shade into the phenomena which are regarded as hallucinations.

Lastly, examples of illusion and hallucination are common during actively progressing cerebral dissolution, as the result of the consequent riot of the processes of lower association which exists in patients suffering from this pathological condition of the cerebrum. Whilst to the observer these phenomena appear from the actions of the patients to possess an objective reality, it is probable in such cases that they are almost or entirely unaccompanied by consciousness, since in such cases extensive dissolution of the prefrontal centre of higher association has, as a rule, already taken place.

It is thus evident that illusion and hallucination grade from, on the one hand, the simple false recognitions of the normal sane individual, to, on the other, vivid associated memories which arise by processes of lower association, in the absence of sensory stimuli, and which, in the

absence of control over the processes of cerebral association, may present such a resemblance to the psychic results of the recognition of sensorial stimuli as to be mistaken for these and projected externally.

Normal illusions thus occupy one end of the series, and the purely psychic phenomena described as hallucinations occupy the other, the numerous intermediate types of illusion possessing greater associational and less sensorial components until pure hallucinatory phenomena are reached.

Such psychic phenomena may occur as the result of a pathological process which is of a temporary nature or which will result in neuronic dissolution; they frequently, however, occur in the absence of active pathological conditions of the cortical neurones.

In the former case, particularly when the pathological process is widespread, considerable mental confusion exists and illusions may occur in association with aberrant sensory stimuli of any kind. It is usual, however, for visual illusions to predominate, because, in such patients, visual stimuli are, as a rule, the more numerous.

In the latter case—namely, in the absence of active pathological states of the cortical neurones, and in the consequent absence of mental confusion—the psychic phenomena, as a rule, occur at night, and are often precipitated by imperfect and aberrant auditory stimuli. The cause of this relative prominence of auditory psychic phenomena appears to be twofold. On the one hand, in at any rate most ordinary individuals, the usual channels for the reception and transmission of knowledge are hearing and speech, sight, except in the case of special psychic acquisitions, occupying a subordinate position. Further, the majority of persons think in words as spoken, rather than in words as seen. On the other hand, at night, and particularly during sleep, the higher cerebral processes are dormant or at their lowest ebb, and in consequence the processes of lower association, if active, are uncontrolled. Again, fear or apprehensiveness is naturally greater at night, or in the dark, than it is by day; and hearing, which is then the only sense available, is therefore preternaturally acute. It is thus possible to give a simple psychological explanation of the prominence of auditory illusions and hallucinations in such types of case as high-grade amentia and non-progressive dementia.

It is impossible here to do more than refer in the briefest manner to those more common symptoms of mental disease of which the physical bases may be relegated without hesitation to the centres of lower association. I shall therefore make no reference to the subject of

delusion in the sane and the insane, or to that interesting and allied question, the recording of experience in a time-related manner. I have merely endeavoured to indicate, in more or less general terms, the relationship which I think exists between the normal processes of lower cerebral association and those which occur in the insane.

Whilst the linking together of such normal and abnormal processes of cerebral association cannot be regarded as evidence in favour of the particular partially proved provisional hypothesis of the cerebral functions which I have attempted to lay before you, such a comparison is, nevertheless, of interest in that it shows that the processes of cerebral association, whether of the sane or of the insane, are equally susceptible of explanation by means of it.

ADDENDUM.

The majority of the cases referred to in these lectures have already been published in previous communications. The essential details concerning these are contained in the following appendices, which also include detailed descriptions of the new cases.

For the use of Case C (Appendix A), a fœtus of 7 to 8 months, I am indebted to Dr. G. A. Watson, who has kindly lent me a series of preparations for photography and measurement. The illustrations of the precentral cortex of the dog, rhesus and man (figs. 62, 63 and 64) are also prepared from specimens lent to me by Dr. Watson.

Cases 1, 2, 3, 4, 5, 6, 7, 12, 13 and 16 (Appendix B) are new, and have been obtained at the Rainhill Asylum through the courtesy of Dr. Wiglesworth. The hemispheres illustrated on figs. 38 to 47 are also from cases who died at Rainhill Asylum. None of these photographs of hemispheres have been specially prepared. They have been selected from the systematic laboratory records—on the one hand because they were suitable cases, in the clinical course of which I was specially interested, and on the other because a series obtained in this manner exemplifies the ease with which abnormal and morbid appearances of the cerebrum may be studied when they have been systematically recorded.

I would remark that the method of recording intracranial appearances which I employed [7] whilst at Claybury Asylum has been adopted by Dr. G. A. Watson, who has used it at Claybury and subsequently at Rainhill. In a paper [26] published since these lectures were delivered, Watson has recorded his observations at Rainhill, and has compared his results with those obtained by myself at Claybury, arriving by a somewhat different mode of reasoning at substantially identical conclusions.

It is worthy of note that these conclusions of Watson have resulted from a study of morbid appearances alone, whereas the chief feature of my own papers was a correlation of the intracranial appearances found after death with the clinical features presented by the cases during life. I, therefore, trust that the definite relationship, which exists between the clinical evidences of amentia and dementia during life and the corresponding indications of cerebral sub-evolution and dissolution which are found after death, will in the future receive fuller recognition than has hitherto been bestowed upon it.

The preliminary acceptance of this general truth, followed by the combined clinical investigation of individual cases and macroscopic and microscopic study of the cerebra of these, is, I am convinced, essential as a scientific basis for the rational study of mental disease.

APPENDIX A.

THE FŒTAL AND INFANTILE BRAINS REFERRED TO IN FIGS. 20 AND 21.

Case A.—Male fœtus, aged a little over four months (fig. 11). Weight of the right hemisphere, after hardening in formalin, 32 grm. The prefrontal cortex of this case is shown in fig. 12.—*Archives of Neurology*, vol. ii., p. 571, Case 4.

Prefrontal Measurements. General average:—I, ·155; II—V, ·677. Total, ·832 mm.

Case B.—Fœtus, aged a little over six months (fig. 13). Weight of the left hemisphere, after hardening in formalin, 55 grm. The prefrontal cortex of this case is shown in fig. 14.—*Ibid.*, vol. ii., p. 572, Case 5.

Prefrontal Measurements. General average:—I, ·118; II, ·221; III, ·118; IV, ·221; V, ·221. Total, ·899 mm.

Case C.—Fœtus, aged between seven and eight months (fig. 15). Weight of the right hemisphere, after hardening in sublimate and formalin, 56 grm. The prefrontal cortex of this case is shown in fig. 16, and the visuo-sensory and visuo-psychic cortices in fig. 24.

Prefrontal Measurements.

Lamina	I	II	III	IV	V
Side (average of 13)	·071	·254	·128	·128	·175
Apex (average of 14)	·075	·360	·154	·200	·255
Bottom (average of 10)	·096	·217	·108	·075	·110
Flat (average of 28)	·072	·359	·155	·161	·216
General average (·841 mm.) ..	·078	·297	·136	·141	·189

Case D.—Right hemisphere of a stillborn male infant (fig. 17). Weight, after hardening in formalin, 194 grm. Left hemisphere, ditto, 196 grm. The prefrontal cortex of this case is shown in fig. 18.—*Ibid.*, vol. ii., p. 573, Case 6.

Prefrontal Measurements. General average:—I, ·188; II, ·434; III, ·154; IV, ·149; V, ·214. Total, 1·139 mm.

Case E.—Hemispheres of a stillborn female infant. Left, after hardening in formalin, 193 grm. Right, ditto, 190 grm.—*Ibid.*, vol. ii., p. 574, Case 7.

Prefrontal Measurements. General average:—I, ·217; II, ·575; III, ·178; IV, ·184; V, ·240. Total, 1·394 mm.

Case F.—Left hemisphere of an infant aged six months. Sex unknown. Died from marasmus. Whether this child was full-term or not it is, of course, impossible to state. It is possible, however, in view of the feeble and emaciated condition of the child, that its cerebral as well as its general bodily development had been retarded. Weight of the left hemisphere, after hardening in formalin, 161 grm.—*Ibid.*, p. 575, Case 8.

Prefrontal Measurements. General average:—I, ·188; II, ·520; III, ·174; IV, ·192; V, ·254. Total, 1·328 mm.

Case G.—Anophthalmos. Born of healthy parents and died from marasmus at the age of one month. The post-mortem was made forty-eight hours after death, in a small country cottage. The orbits were chink-like, and contained a little yellowish tissue at the back, which was apparently composed of fat. The eyelids were represented by small slits. No trace of either optic nerves or eyeballs could be discovered. A drawing of the visuo-sensory area is given as Case 6 in fig. 9.—*Phil. Trans.*, B 191, 1900, p. 202.

Visuo-Sensory Measurements.—General average:—I, ·221; II, ·454; III*a* and III*b*, ·296; III*c*, ·223; IV, ·195; V, ·215. Total, 1·604 mm.

Visuo-Psychic Measurements. General average:—I, ·195; II, ·530; III, ·164; IV, ·254; V, ·208. Total, 1·351 mm.

Case H.—A perfectly healthy male infant, who died at the age of three months from broncho-pneumonia. A drawing of the visuo-sensory area is given as Case 5 in fig. 9.—*Ibid.*, p. 201.

Visuo-Sensory Measurements. General average:—I, ·243; II, ·428; III*a*, ·221; III*b*, ·241; III*c*, ·243; IV, ·141; V, ·202. Total, 1·719 mm.

Visuo-Psychic Measurements. General average:—I, ·242; II, ·676; III, ·191; IV, ·212; V, ·224. Total, 1·545 mm.

APPENDIX B.

NOTES OF THE THIRTY CASES REFERRED TO IN FIGS. 57 AND 58.

Case 1.—A male idiot who was admitted at the age of 10 and died at the age of 27. No history. Epileptic. "Cannot understand what is said to him, but stares vacantly when spoken to. Runs aimlessly about the wards and yards, and takes no notice of what is happening around. Laughs fatuously at anything, and performs monotonous, purposeless movements of the hands. Is inattentive to the calls of nature and cannot feed himself."

On admission was restless, wriggling about like an eel. Would not speak, but made inarticulate noises and said the word "yes" once, but not in any articulate sense. Was wet and dirty, and had to be dressed. He recognised people and showed a great variety of emotions—e.g., pleasure, anger, and grief.

A year before his death his condition had somewhat altered. Appearance vacuous, forehead receding, chin projecting. Hands cold and blue and showing signs of prolonged disuse. Skin rough. He made "negative" movements with his head almost constantly, and had a habit of balancing himself on one foot and the other alternately. In walking he shuffled along with his toes out and tended to drag the right foot. He did not understand what was said to him and could not speak. He could imitate the actions of other patients, but he had no idea of holding a pencil. He had a habit of making queer laughing noises through his shut lips. He could feed himself and used to grab at food. He was a "nice" boy, and showed none of the spitefulness so often seen in idiots, particularly when epileptic. He had 52 fits during the 15 months following his admission, and none during the following 18 years.

He died from tuberculosis of the lungs and intestines.

Encephalon 1133 grm., R.H. 490 grm., L.H. 485 grm., stripped 465 grm. Intracranial appearances natural apart from a moderate excess of subdural fluid. Brain below natural size, nearly proportionately developed, and of a convolutional pattern, which is rather below the average.

MICROMETRIC MEASUREMENTS OF CASE 1.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·183	·467	·153	·180	·245	·118	·189
Apex	·134	·355	·146	·217	·298	·166	·374
Bottom	·368	·421	·141	·127	·156	·059	·094
Flat	·125	·342	·144	·202	·292	·153	·280
General Average	·203	·396	·146	·182	·248	·124	·234
				·576			

1·533 mm.

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·175	·875	·237	·183	·255
Apex	·133	·751	·271	·318	·463
Bottom	·346	·655	·166	·081	·118
Flat	·153	·844	·247	·227	·321
General Average	·202	·781	·230	·202	·289

1·704 mm.

Case 2.—A male imbecile of moderate grade, with epilepsy. Admitted at the age of 12 and died at the age of 17 years. No history. "Imbecile. Claps his hands. Is 'boss' of this place. Does not know where he is. Laughs when spoken to. Very excited at times. Throws his boots at people. Unmanageable."

On admission was imbecile and fatuous. Possessed some memory and knew where he was, when he came, and the day of the week. Could remember being in another asylum for three years. Continually laughed, made grimaces and clapped his hands. Said that he had fits sometimes, and had had the last one two months ago.

Six months after admission he had 17 fits in a month, and four more during the next three months. He had no more fits until nine months before his death, when he had one. Before these fits he was a passably good boy, but afterwards he became more and more excitable, mischievous, troublesome and destructive, right up to the time of his death.

Two years before his death his condition was as follows:—Head small, especially in the frontal region. Vacant expression and the appearance of a child. Teeth pointed. A gap between the central incisors. He spoke with a lisp, and gave a fair but simple account of himself. He was fairly correct in his dates. He stated that he had been to school and had got into Standard II. $2 \times 3 = 6$, $4 \times 3 = 9$. He could not spell "cow," but then voluntarily remarked "c-a-t, cat." He slowly and painfully wrote his name, missing out the last vowel from each of the words. He seemed very pleased with this effort. He smiled pleasantly and seemed a very good and nice boy.

He was, however, one of the worst boys who had been in the asylum. He was filthy in his habits, untidy, destructive out of wantonness, very mischievous, and had quite a marvellous flow of foul language. He was by far the worst swearer in the asylum. He died from broncho-pneumonia and gangrene of the lungs, together with chronic dysentery.

Encephalon 995 grm., R.H. 444 grm., L.H. 440 grm., stripped 420 grm. There were no intracranial morbid appearances and the brain was considerably below the average size. The cerebellum weighed but 108 grm. The pattern of the cerebral hemispheres was generally simple, especially in the prefrontal region, and the sulci were generally shallow.

Micrometric Measurements of Case 2.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·165	·445	·147	·239	·290	·093	·181
Apex	·152	·317	·140	·240	·298	·158	·321
Bottom	·221	·395	·143	·203	·231	·074	·133
Flat	·108	·290	·150	·243	·290	·133	·228
General Average	·162	·362	·145	·231	·277	·115	·216
1·508 mm.				·653			

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·187	·731	·227	·195	·258
Apex	·152	·728	·275	·317	·408
Bottom	·299	·602	·164	·087	·147
Flat	·144	·582	·218	·287	·349
General Average	·196	·661	·221	·222	·291
1·591 mm.					

Case 3.—A male imbecile of moderate grade, with epilepsy. Admitted at the age of 26 and died at the age of 32. He was stated to have shown symptoms from the age of six years and he had been in a workhouse since the age of 20 years. No history. "Sullen, resentful, accusing all the inmates and attendants of abusing him (untrue), and wants to strike them. Kicks without warning all who approach him."

On admission was imbecile and very fatuous. Attention poor. Very incoherent and irrational. No idea of position and surroundings, and incapable of appreciating the lapse of time. Did not know where he was or whence he had come. No idea of the day of the week or the month. Could not tell his age. Knew that he took fits, but could not say when the last one occurred.

From a history which was subsequently obtained it appeared that when between 6 and 7 years of age he began to take fits. His education was neglected after this; and he ran about the streets, and had frequent and severe fits. He was always very simple-minded. He eventually became so mischievous that he had to be removed to the workhouse.

During his residence he had about 12 fits a month, which were rarely, if ever, followed by excitement. He was dirty and untidy and would not work. He was very violent at times, would strike out at anyone, and used often to smash plates and cups during meals. He could not, or would not, give any account of himself. He usually replied "nothing" or "nowhere" to questions, or gave such incoherent replies as "Oh, 38 T—— Street, not long. Seen Uncle John." He scrawled with a pencil, but made no attempt to write letters. He appeared to have no initiative as a rule, but it was impossible to be certain whether he was obstinate or simply dull. He died from pneumonia and gangrene of the lungs.

Encephalon 1180 grm., R.H. 515 grm., stripped 497 grm., L.H. 495 grm. Cerebellum 150 grm. No intracranial morbid appearances. The hemispheres were below the average complexity in pattern, and the sulci were shallow.

Since the death of this patient his brother has been admitted, suffering from an acute attack of mania without confusion. He is an excited, violent, impulsive and very dangerous case.

Micrometric Measurements of Case 3.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·242	·492	·181	·264	·280	·103	·209
Apex	·149	·372	·153	·315	·320	·175	·339
Bottom	·339	·480	·164	·151	·178	·060	·122
Flat	·162	·402	·159	·324	·298	·180	·314
General Average ..	·223	·437	·164	·264	·269	·130	·246

1·733 mm. ·697

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·208	·654	·202	·169	·249
Apex	·141	·580	·232	·296	·382
Bottom	·348	·517	·134	·074	·133
Flat	·136	·505	·211	·273	·365
General Average ..	·208	·564	·195	·203	·282

1·452 mm.

Case 4.—A male, suffering from a moderate grade of imbecility together with premature dementia. Admitted at the age of 21 and died at the age of 29. Was in an asylum from 15 to 18, and in a workhouse from 18 to 21. "Patient thinks people wish to do away with him by making him eat carbolic soap, and has tried to climb walls to get away because of the above. Is always shouting and crying."

He showed signs of phthisis on admission. He was imbecile and fatuous. He lay quietly in bed and submitted readily to examination. He was incapable of appreciating his position and surroundings or of accurately gauging the lapse of time. He could not tell where he was or whence he came, or the day of the week or the month. He answered very badly to questions and could give hardly any account of himself. He said that he had had fits for years. He stated that he had been in an asylum for five years and in a workhouse for three years, where an attendant encouraged him to drink the soap, and kicked him.

When he had got settled in the asylum he was restless, excited, talkative, and frightened. He could give a fairly good account of himself. He recognized some letters but could not read the simplest words. He could count up to 12 and name simple colours correctly. He could name ordinary articles.

He called a thermometer a "ventilator to tell the heat of the room." He could dress himself, but did not work.

Two years before his death his condition had somewhat changed. Lobules of ears adherent. Palate very high and shelving, and narrow. Teeth small and ground down. He keeps his hands in his pockets. He writes an unintelligible scrawl, which seems to be an imitation of writing by one who has never been able to properly learn. He has a lisp. He gives his name and many of the letters of the alphabet. 2 × 2? "Twice is 2, twice 2 is 2, twice is 2 2." 5 × 2? "Is six." 3 × 2? "Is 10, isn't it?" He went to school and got into the standard "where they draw the slates and sit at tables with pencils and write in copybook." Work? "I used to make brushmaking with wire on a vice and we used to . . . and I can glue in brushes what they sweep the floors with, with a handle to." Age? "Well, I don't know, well, I think, Sir, 60, over 60 I think, 80, 80." Here long? "I was here, I was here longest man in place. There wasn't a patient here when I come. There was only fields and no bricks, and no houses, and a man was knocking the door down with nails." He gives the day wrongly and also the date, saying, "16th, isn't it? Saturday, 16 October, April or May." He was excited and hysterical at times and was incapable of employment. He died from tuberculosis of the lungs and intestines.

Encephalon 1235 grm., R.H. 550 grm., L.H. 530 grm., stripped 514 grm. Cerebellum 150 grm. Moderate excess of fluid. Strips fairly readily. The cerebral hemispheres are below the average size and are a little below the average complexity of pattern, especially in the prefrontal region. There is slight and general fronto-parietal wasting.

Micrometric Measurements of Case 4.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·209	·567	·209	·255	·290	·106	·194
Apex	·177	·380	·152	·305	·320	·172	·336
Bottom	·289	·386	·156	·200	·214	·066	·136
Flat	·206	·449	·171	·334	·300	·199	·321
General Average	·220	·446	·172	·274	·281	·136	·247
1·776 mm.				·727			

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·149	·626	·208	·153	·221
Apex	·103	·704	·247	·339	·449
Bottom	·312	·486	·138	·062	·102
Flat	·181	·884	·295	·293	·383
General Average	·186	·675	·222	·212	·289

1·584 mm.

Case 5.—Female, widow, forewoman, aged 50. Duration before admission, 10 days. She died from infective endocarditis after a residence of 22 days. "Patient is in a state of acute mania. She screams and talks incoherently day and night. Has to be fed by force. Says she is the King's daughter."

Apical systolic murmur. Feeble health. Very noisy, incoherent and restless. Very resistive. Refuses food. Talks incessantly. Cannot give any account of herself. Is dirty in habits. Sleeps very little, and is very destructive to her bedding.

Encephalon 1245 grm., R.H. 540 grm., L.H. 535 grm., stripped 496 grm. Cerebellum 162 grm. Intracranial contents œdematous. Moderate excess of fluid. Membranes normal. Brain below average female weight. Pattern decidedly simple in the prefrontal region, and below the average in the parietal region.

MICROMETRIC MEASUREMENTS OF CASE 5.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·224	·496	·159	·299	·298	·143	·213
Apex	·131	·339	·140	·276	·318	·168	·376
Bottom	·318	·407	·141	·191	·199	·070	·112
Flat	·155	·526	·152	·292	·295	·166	·255
General Average	·207	·442	·148	·265	·278	·137	·239
1·716 mm.				·691			

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·199	·825	·219	·183	·252
Apex	·174	·734	·242	·415	·501
Bottom	·337	·591	·155	·085	·130
Flat	·159	·731	·212	·197	·286
General Average	·217	·720	·207	·220	·292
1·656 mm.					

Case 6.—Male, married, dock labourer, aged 25. Duration before admission five weeks. Died from pneumonia after a residence of 38 days. "Active melancholia. Profoundly depressed, actively suicidal, refuses to speak. Has recent marks on his neck from a knife."

Maternal grandmother had religious mania. Patient never touches drink. His nerves were upset owing to an accident 11 months ago, and he became melancholic and was always complaining about his stomach. He worried a good deal about his work and gave it up 5 to 6 weeks ago.

On admission patient had sordes on the lips and teeth, and a purulent discharge from the urethra. Very depressed. Takes no notice of anything, and occasionally makes a slight moaning noise. Is very restless and often tries to get out of bed, struggling aimlessly if interfered with. He gives his name in a

whisper, but no further replies to questions. He takes no notice of food, but swallows it when fed with a spoon. He is clean in his habits. Two days after admission patient tried to strangle himself with a scarf. A week later he was very dull, depressed and agitated. He resisted everything done for him and needed treatment in the padded room. He frequently called out the same phrases over and over again. At the time of his death he showed slight mental improvement.

Encephalon 1570 grm., R.H. 695 grm., L.H. 690 grm., stripped 652 grm. Cerebellum 175 grm. Slight excess of fluid. Strips readily. The brain is considerably above the average size. There is decreased development of the prefrontal region, and asymmetry on the two sides with regard to the relative development of the different regions of association. On the whole the pattern is below the average complexity.

Micrometric Measurements of Case 6.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·200	·467	·159	·252	·292	·137	·228
Apex	·219	·446	·152	·283	·300	·215	·384
Bottom	·271	·435	·144	·173	·219	·080	·147
Flat	·205	·426	·153	·255	·295	·180	·283
General Average	·224	·444	·152	·241	·277	·153	·261
1·752 mm.				·670			

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·196	·754	·222	·161	·242
Apex	·203	732	·253	·340	·505
Bottom	·321	.572	·150	·074	·133
Flat	·222	·913	·280	·262	·359
General Average	·236	·743	·226	·209	·310
1·724 mm.					

Case 7.—Female, single, servant, aged 30. Duration before admission two weeks. Died from cancer of the lung after a residence of nine months. Parents both intemperate.

Thirteen years ago patient had an attack of melancholia, and was treated in the workhouse. Since that time she has been a general servant, has kept well, and has worked steadily. She suddenly became noisy and excited about two weeks before admission. "Noisy, excited and incoherent. Requires to be restrained, and is trying to be free. Violent, noisy and dirty."

On admission, the patient, who is a nullipara, was very restless, emotional and excited. She made grimaces, gesticulated, and was quite incoherent. When asked to write her name she took the pencil and wrote her initials, but then at once broke away and scrawled all over the paper, at the same time

laughing and talking incoherently. She was extremely emotional, laughing and crying by turns, and using foul language very frequently. She noticed everything around her and frequently repeated what she happened to hear. At times she listened as if to voices, and made such remarks as "You're a liar," "I never was drunk in my life," "Mother's over there." At times she threw crockery and struggled if prevented. She was very noisy at night, singing and shouting. She was very troublesome and resistive over her food, and she was wet and dirty in her habits.

Towards the time of her death, though she was still excitable, and noisy at night, and appeared to suffer from hallucinations of hearing, she was often quite sensible. She talked intelligently to her friends. She asked the nurses for forgiveness for all she had said and done to them. She was very clean in her habits, and, when more feeble, used to get into an awful state if she happened unavoidably to "make a mistake." From the beginning to the end of her illness, whilst at first all the nurses with whom she was in contact could not get on with her, they invariably ended in being extremely fond of her.

Encephalon 1555 grm., R.H. 670 grm., L.H. 672 grm., stripped 645 grm. Slight excess of fluid. Pia stripped rather more readily than natural. Cerebellum 195 grm. The brain was much above the average female size. The cerebrum was very complex, and many secondary gyri were present.

MICROMETRIC MEASUREMENTS OF CASE 7.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·261	·629	·227	·346	·308	·144	·242
Apex	·197	·446	·166	·355	·313	·214	·415
Bottom	·306	·535	·150	·202	·211	·078	·122
Flat	·239	·595	·186	·230	·295	·141	·230
General Average	·251	·551	·182	·283	·282	·144	·252
				·747			

1·945 mm.

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·222	·935	·253	·208	·284
Apex	·166	·829	·261	·370	·520
Bottom	·331	·567	·152	·088	·140
Flat	·161	·950	·273	·321	·420
General Average	·220	·820	·235	·247	·341

1·863 mm.

Case 8.—Male, aged 55. Normal.—*Phil. Trans.*, B 191, 1900, page 188, Case 1.

Micrometric measurements of Case 8:—

Visuo-Sensory. General average:—I, ·254; II, ·523; III*a*, ·218; III*b*, ·215; III*c* ·289; IV, ·142; V, ·240. Total, 1·881 mm.

Visuo-Psychic. General average :—I, ·274 ; II, ·864 ; III, ·200 ; IV, ·229 ; V, ·293. Total, 1·860 mm.

Case 9.—Female, aged 17. A case of epileptic dementia.—*Ibid.*, page 192, Case 2.

Micrometric measurements of Case 9 :—

Visuo-Sensory. General average :—I, ·227 ; II, ·423 ; III*a*, ·224 ; III*b*, ·238 ; III*c*, ·299 ; IV, ·146 ; V, ·265. Total, 1·822 mm.

Visuo-Psychic. General average :—I, ·248 ; II, ·778 ; III, ·207 ; IV, ·213 ; V, ·290. Total, 1·736 mm.

Case 10.—Female, aged 27. A case of blindness from infancy, and chronic insanity with dementia.—*Ibid.*, page 195, Case 3.

Micrometric measurements of Case 10 :—

Visuo-Sensory. General average :—I, ·235 ; II, ·396 ; III*a*, ·198 ; III*b*, ·112 ; III*c*, ·270 ; IV, ·120 ; V, ·250. Total, 1·581 mm.

Visuo-Psychic. General average :—I, ·250 ; II, ·791 ; III, ·222 ; IV, ·182 ; V, ·297. Total, 1·742 mm.

Case 11.—Male, aged 30. A case of long-standing blindness, and chronic insanity with dementia.—*Ibid.*, page 198, Case 4.

Micrometric measurements of Case 11 :—

Visuo-Sensory. General average :—I, ·281 ; II, ·418 ; III*a*, ·193 ; III*b*, ·136 ; III*c*, ·291 ; IV, ·129 ; V, ·219. Total, 1·667 mm.

Visuo-Psychic. General average :—I, ·289 ; II, ·768 ; III, ·178 ; IV, ·194 ; V, ·248. Total, 1·677 mm.

Case 12.—Male, single, packer, aged 23. Maternal aunt in an asylum. Mother dull and slow, and of poor memory. Father and mother intemperate. Youngest sister left school at the age of 14 after entering Standard VI. Patient was in Standard VI at the age of thirteen and-a-half, and then refused to go to school any longer. He was then in Ireland for six months, was then for six months in a printing works, and was afterwards in a mill for five years. He then suffered from appendicitis, but did not require operation. After leaving the hospital he worked at a mill until three days before admission to the asylum. "When he came home from work, he started laughing and acted in a silly manner." He did not drink.

"Delusions that he is being transformed into a 'Jap.' Uses foul language when spoken to. Shakes his fist at the skylight as if threatening someone. Excited, noisy, violent, and refuses food at times. Dirty."

On admission he was pale and thin. Ears plain. Pinnæ large. Palate high. Alveolus very thick. Slight double internal strabismus. Phimosis. Excited, restless, noisy and garrulous. Gesticulates and strikes attitudes. Slaps the bed and parts of his body. Very theatrical in behaviour. Talks about "God," "Man-God," and "Buffalo Bill holding the whole world in his hand." A sequence of ideas can be traced. He gives his name and age, and adds "twenty-two summers, never known death and never will," and then talks

about Father, Son, and Holy Ghost, &c. At times he answers questions, and at others does not. His attention can be attracted for the moment, and then after replying he becomes inconsequent, and afterwards incoherent. Day? "My birthday, 22 December." Where are you? "I'm in Liverpool now, Scotland Yard. Detective." Name of head attendant? "Mr. Steward or some great man at B——. I being a scamp and a fool along the docks. Another Christian man. All Christianity has been a blaspheming from beginning to end." He is restless, noisy, impulsive, and wet and dirty. He sleeps and takes his food.

During the first month after his admission he made several temporary recoveries. A week later he tied a scarf tightly round his neck. Three months after his admission he was constantly restless, excited, incoherent, monkey-like, and unemployed. He then gradually improved during five months, and became a worker. Eight months after his admission he gradually developed stupor. He spoke slowly and with a long latent period. His face became greasy and expressionless. At times, when spoken to, he appeared to brighten up, but soon relapsed into stupor. He remained in this condition until his death, eighteen months after admission, becoming cold and blue and thin, and eventually dying from marasmus.

Encephalon 1435 grm., R.H. 605 grm., stripped 570 grm., L.H. 608 grm. Cerebellum 215 grm. Intracranial morbid appearances of moderate intensity, (Group III). Smaller cerebral vessels wiry. Hemispheres of average size but below average complexity. Gyri generally large. Some prefrontal wasting,

MICROMETRIC MEASUREMENTS OF CASE 12.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·246	·527	·171	·217	·267	·127	·208
Apex	·199	·471	·166	·247	·298	·188	·350
Bottom	·306	·471	·140	·162	·180	·066	·107
Flat	·199	·527	·155	·239	·295	·177	·269
General Average ..	·238	·499	·158	·216	·260	·140	·234
1·745 mm.				·634			

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·242	·809	·208	·180	·249
Apex	·169	·744	·230	·289	·431
Bottom	·328	·652	·133	·074	·140
Flat	·183	·787	·222	·267	·330
General Average ..	·231	·748	·198	·203	·288
1·668 mm.					

Case 13.—Male, single, plumber, aged 44. No history. "Memory a blank. Can remember nothing that has happened. Does not know when he had food last. He says that he has had none to-day and that he has not much inside left. Depressed and silent and takes little notice of anything."

On admission: Palate high and shelves forwards. Face expressionless. Speech occasionally slurred. Knee-jerks absent. Pupils below medium and react rapidly to light and accommodation. Early tuberculosis of lungs.

Dull and apathetic. Gives his name. Age, "63 . . . 61, I beg your pardon." Knows neither the day, the date, the month, nor the year. Does not know when he came. At different times he gave his age as "63 come Christmas," "35," and says he was born in the year "1860" (correct). He denies venereal disease, having been "one of the lucky ones." He says that he has always come off "second best at anything I've tackled." He has drank a good deal. At times he brightens up during conversation, but he rapidly lapses into silence and he never volunteers a remark. He appears not to suffer from either illusions or hallucinations.

Six months after admission he was dull and took little interest in his surroundings. He could give no account of recent events. His conversation was coherent, but his memory, especially for recent matters, was very poor. In the month of November he thought that it was summer. He remarked that his memory was bad, but that it was slowly coming back again.

Six months later he gave his age as 60. He stated that he came a fortnight ago, and was ignorant of such recent events as even an ordinary case of dementia might have been expected to remember. He knew me but not my name, although he had known me well since his admission.

He died from tuberculosis of the lungs and intestines twenty-one months after admission, at which time he was practically a skeleton. He exhibited well-marked but not gross dementia, which was, however, unusually profound for a man of his age who did not suffer from general paralysis.

Encephalon 1260 grm., R.H. 525 grm., L.H. 522 grm., stripped 488 grm. Cerebellum 178 grm.

Enormous excess of fluid. Pia stripped extremely readily. Cerebral hemispheres—below the average size, and perhaps so even when wasting was allowed for: proportionately developed; rather below the average complexity. Convolutions rather small, especially in the prefrontal region. Wasting very marked in the fronto-parietal and upper temporal regions, but especially severe in the prefrontal region. The wasting appears to be of an unusually pure neuronic type, since the cerebral vessels, large and small, are quite normal. A recent subdural deposit of the thickness of brown paper.

Micrometric Measurements of Case 13.

Visuo-Sensory.

Lamina	I	II	III			IV	V
			a	*b*	*c*		
Side	·228	·617	·269	·299	·295	·177	·273
Apex	·166	·436	·151	·357	·318	·230	·407
Bottom	·331	·465	·147	·172	·206	·075	·124
Flat	·155	·445	·155	·300	·305	·191	·298
General Average	·220	·491	·166	·282	·281	·168	·276
				·729			

1·884 mm.

Visuo-Psychic.

Lamina	I	II	III	IV	V
Side	·197	·798	·240	·171	·236
Apex	·175	·794	·274	·362	·516
Bottom	·380	·613	·158	·094	·137
Flat	·189	·815	·250	·254	·362
General Average	·235	·755	·231	·220	·313

1·754 mm.

Prefrontal.

Lamina	I	II	III	IV	V
Side	·225	·694	·234	·181	·256
Apex	·141	·681	·277	·387	·482
Bottom	·320	·566	·180	·092	·143
Flat	·146	·608	·250	·306	·409
General Average	·208	·637	·235	·242	·323

1·645 mm.

Case 14.—Female, aged 36. A case of well-marked imbecility. Brain rather small but perfectly natural, except for slight simplicity of pattern and a somewhat decreased development of the prefrontal region. Weight 1165 grm. —*Archives of Neurology*, vol. ii., p. 579, Case 9.

Prefrontal Measurements. General average :—I, ·209 ; II, ·526 ; III, ·163 ; IV, ·189 ; V, ·257. Total, 1·380 mm.

Case 15.—Female, aged 24. A case of well-marked imbecility with epilepsy, of a rather milder grade than the preceding case. Cerebrum very small, 660 grm. Pattern fairly normal. Marked mycrogyria in the upper third of the external surface of each hemisphere near the median fissure but not involving the median portion of the hemispheres. The cuneus is represented by a single gyrus, and the cuneal annectant runs superficially into the cingulate gyrus.—*Ibid.*, p. 582, Case 10.

Prefrontal Measurements. General average :—I, ·253 ; II, ·607 ; III, ·193 ; IV, ·215 ; V, ·281. Total, 1·549 mm.

Case 16.—A male macrocephalic imbecile of moderate grade. Age unknown, but probably about 50. Had been certified 37 years at death, and was in the present asylum fourteen years. Height, 58½ in. Circumference of head, 23¼ in. Small body and limbs. Childish and of low intelligence. Vocabulary limited, and the words used to express his wants are indistinctly uttered and helped out for the comprehension of others by signs. Fond of attention. Voracious and eats ravenously and rapidly. Clean in habits when watched, but requires tending. He could dress himself. He was destructive and impulsive and fond of annoying feeble old men who might be expected to be unable to retaliate. He used to shout when an officer entered the ward, and was accustomed to ask for a basin of tea before going to bed. He was a favourite with the staff, who taught him to sing songs and to repeat new words. He died from mitral stenosis and gangrene of the lung.

Encephalon 1775 grm., R.H. 816 grm., stripped 775 grm., L.H. 775 grm., stripped 747 grm. Cerebellum, 180 grm. White matter firmer than normal. Corpus callosum short and thick. Intracranial morbid appearances slight or absent (Group I-II). Arrangement of gyri very complex and very irregular. Sulci deep. Convolutions of good size and breadth, with the exception of the frontal and parietal regions, where some are very good and some are very poor. The parietal region is relatively very small, as are also the gyri in this region. The normal distribution of the main sulci cannot be made out, as these are largely replaced by numerous curved gyri.

Prefrontal Measurements. General average:—I, ·278; II, ·663; III, ·212; IV, ·236; V, ·295. Total, 1·684 mm.

Case 17.—Female, aged 11. A case of mild imbecility with epilepsy who might have been capable of considerable improvement under proper training. Encephalon 1100 grm. Some under-development of the prefrontal region near the midline, most evident in the left hemisphere. This is not marked, and on ordinary examination the brain would readily pass for normal. *Archives of Neurology*, vol. ii., p. 583, case 11, right hemisphere.

Prefrontal Measurements. General average:—I, ·276; II, ·729; III, ·201; IV, ·193; V, ·272. Total, 1·671 mm.

Case 18.—Ditto. Left hemisphere.

Prefrontal Measurements. General average:—I, ·290; II, ·770; III, ·199; IV, ·199; V, ·274. Total, 1·732 mm.

Case 19.—Female, aged 56. A case of recurrent insanity of a duration of fifteen days in the asylum, and perhaps a few months outside. Brain normal, weight 1185 grm.—*Ibid.*, p. 591, Case 13.

Prefrontal Measurements. General average:—I, ·261; II, ·701; III, ·212; IV, ·216; V, ·302. Total, 1·692 mm.

Case 20.—Female, aged 49. A case of chronic insanity without dementia. Brain normal apart from an old-standing softening in the right hemisphere, probably due to embolic occlusion of the middle cerebral artery. Encephalon 1115 grm.—*Ibid.*, p. 592, Case 15.

Prefrontal Measurements. General average:—I, ·259; II, ·723; III, ·212; IV, ·209; V, ·293. Total, 1·696 mm.

Case 21.—Female, aged 36. A case of chronic insanity with little or no dementia. Cerebrum 1235 grm. Very slight intracranial morbid appearances. Hemispheres normal. *Ibid.*, p. 591, Case 14.

Prefrontal Measurements. General average:—I, ·264; II, ·754; III, ·231; IV, ·229; V, ·308. Total, 1·786 mm.

Case 22.—Female, aged 36. Normal. Cerebral small and underdeveloped. Unstripped hemispheres, after hardening in formalin, weighed but 469 and

465 grm. The case may have been one of potential insanity, especially as no history of insanity was looked for.—*Ibid.*, p. 566, Case 3.

Prefrontal Measurements. General average :—I, ·283; II, ·756; III, ·226; IV, ·232; V, ·317. Total, 1·814 m.m.

Case 23.—Female, aged 38. Normal. After hardening in formalin, the right hemisphere weighed 539 grm., and the left 515 grm., both unstripped.—*Ibid.*, p. 565, Case 1.

Prefrontal Measurements. General average :—I, ·277; II, ·836; III, ·241; IV, ·236; V, ·302. Total, 1·892 mm.

Case 24.—Male, aged 13. Normal. Stated to be deaf and dumb. After hardening in formalin, R.H. weighed 577 grm., and L.H. 568 grm.—*Ibid.*, p. 566, Case 2.

Prefrontal Measurements. General average :—I, ·341; II, ·901; III, ·220; IV, ·223; V, ·310. Total, 1·995 mm.

Note.—As an increase in weight, to the extent of about 10 per cent., takes place during the process of hardening in formalin, the above three normal cases (Cases 22, 23, and 24) all have brain weights which are well below the average, and are consequently likely to give micrometric results which are below rather than above the average normal.

Case 25.—Male, aged 37. A case of imbecility with mild dementia. Slight intra-cranial morbid appearances. Encephalon 1305 grm.—*Ibid.*, p. 588, Case 12.

Prefrontal Measurements. General average :—I, ·252; II, ·674; III, ·208; IV, ·200; V, ·290. Total, 1·624 mm.

Case 26.—Female, aged 59. A case of mania with marked dementia. Intracranial morbid appearances of moderate intensity (Group III). Encephalon 1220 grm. Cerebral wasting which is marked in the prefrontal region, moderate in the fronto-parietal region and the first temporal gyrus, and slight or absent elsewhere.—*Ibid.*, p. 598, Case 16.

Prefrontal Measurements. General average :—I, ·248; II, ·698; III, ·202; IV, ·208; V, ·292. Total, 1·648 mm.

Case 27.—Female, aged 53. A case of severe dementia. Well-marked intracranial morbid appearances (Group IV). Encephalon 1112 grm. Cerebral wasting which is very severe in front of the ascending frontal gyrus, and moderate over the rest of the fronto-parietal region and the first temporal gyrus, being slight or absent elsewhere.—*Ibid.*, p. 599, Case 17.

Prefrontal Measurements. General average :—I, ·257; II, ·687; III, ·218; IV, ·225; V, ·293. Total, 1·680 mm.

Case 28.—Female, aged 78. A case of gross dementia. Gross intracranial morbid appearances (Group V). Encephalon 1175 grm. Cerebral wasting, which

is very marked in the prefrontal region, well marked in the fronto-parietal region and the first temporal gyrus, and less marked elsewhere.—*Ibid.*, p. 600, Case 18.

Prefrontal Measurements. General average:—I, ·238; II, ·688; III, ·213; IV, ·197; V, ·255. Total, 1·591 mm.

Case 29.—Female, aged 53. A case of gross dementia with Huntington's chorea. Gross intracranial morbid appearances (Group V). Encephalon 1025 grm. The cerebrum shows wasting which is very extreme in the prefrontal region, marked in the fronto-parietal region and the first temporal gyrus, and moderate elsewhere.—*Ibid.*, p. 603, Case 19.

Prefrontal Measurements. General average: I, ·297; II, ·631; III, ·182; IV, ·174; V, ·226. Total, 1·510 mm.

Case 30.—Male, aged 41. A case of gross dementia paralytica. Gross intracranial morbid appearances, together with the usual signs of general paralysis. Encephalon 1280 grm. The brain, after hardening in formalin, cuts like soft wood. The wasting is very extreme in the prefrontal region, it is marked in the central convolutions, it is marked and the morbid process is acute in the parietal region and the whole of the temporo-sphenoidal, and it is moderate in the rest of the cerebrum.—*Ibid.*, p. 608, Case 20.

Prefrontal Measurements. General average:—I, ·274; II, ·682; III, ·168; IV, ·142; V, ·201. Total, 1·467 mm.

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DOES POLIOMYELITIS OCCUR DURING INTRA-UTERINE LIFE?

BY FREDERICK E. BATTEN, M.D.

Introduction.

The object of this paper is to discuss the possibility of the infection of a child with poliomyelitis whilst still *in utero* and to bring forward some evidence that such infection does occur. It must be admitted that there is great difficulty in the differential diagnosis of cases of injury to the nerves of the brachial plexus and of hæmorrhage into the grey matter of the spinal cord of new-born infants from cases of poliomyelitis.

The cases submitted for consideration are cases in which a pathological examination has shown that the condition is due to a lesion of the spinal cord, and had fallen with special incidence on the grey matter of the ventral horns.

Flaccid paralysis of one arm due to birth-injury is far from uncommon in infants, and it has been shown by Herbert Spencer [5] that hæmorrhage into the grey matter of the spinal cords of children dying at birth or soon after delivery is not uncommon. That some of these latter cases in which the hæmorrhage has been less extensive might live has to be considered, and I have seen a case in which such a lesion seemed probable; but I have never been able to prove the condition by pathological examination.

I have only been able to find one reference in the literature to the occurrence of fœtal poliomyelitis, and that is a case published by Fritsch, of Breslau [3]. In that case the child was born without injury, but the birth was a breech presentation. The child had paralysis of both upper and lower extremities. There was a complete atrophic paralysis of both arms, with great loss of electrical excitability, whilst the legs were abducted to the fullest extent at the hips, flexed at an acute angle at the knee, so that the clumped feet lay opposed to one another. The muscles of the legs were not atrophic and responded normally to electrical stimulation. On clinical grounds alone I should not be prepared to

consider the probability of this case being one of poliomyelitis; the spastic condition of the legs is a most unusual symptom in poliomyelitis, and it is one which is extremely likely to occur after a traumatic lesion of the cervical region of the spinal cord. This case is not confirmed by any pathological examination, and therefore may be left aside.

From time to time cases of paralysis in infants have come under observation which from their clinical features suggest the diagnosis of poliomyelitis, and in which the condition is said to have been present at, or immediately after, birth.

Such a history suggests the possibility of an intra-uterine poliomyelitis; it is but seldom, however, that an opportunity arises of proving such a condition by a pathological and microscopical examination. The two cases about to be narrated are of different value from the clinical point of view, for the first was seen when two years old and watched for several years, and always regarded as a case of intra-uterine poliomyelitis; the second, although the paralysis was stated to be present at birth, yet on careful inquiry it was found that the child had not been cared for by its mother during the whole period, but had been in an infirmary: the history is therefore not trustworthy.

Clinical and Pathological Examination of Case 1.

The first case is that of a boy, who, when first seen at the Children's Hospital, Great Ormond Street, in November, 1900, was two years old. The mother, a careful woman, and one whose evidence can, I think, be accepted, gave the following history:—

The child was the second of two children, the first being quite healthy.

At birth it was noticed that the child had weakness of the left arm, but no weakness of the legs was noticed until between the first and second years of life, when the child should have made some attempt to stand.

The birth was natural, but very rapid—labour lasting only twenty minutes—and the child fell from the bed on to the floor. The mother had no illness whilst carrying the child.

There was no history of acute illness during the child's life, and he had had none of the acute specific fevers.

On examination, the child was small and delicate, but of normal intelligence. He could talk, but was quite unable to walk. He could sit up, and used his right hand and arm well. His back was straight.

The left arm hung flaccid from the shoulder, and he had complete paralysis of the left deltoid and biceps, with weakness of the triceps and supinator longus. The muscles of the forearm and hand were relatively well developed, and all movements were capable of being performed. The paralysed muscles were quite flaccid and the head of the humerus hung away from the glenoid cavity. There was some wasting of the scapular muscles.

Both legs were weak, but the right was much more affected than the left, the skin was blue and cold, and in this particular also the right was more affected than the left. The muscles of the right leg were wasted, and especially so below the knee; the gastrocnemius was almost powerless, and the foot assumed a position of pes calcaneus. There was general flaccidity of this limb. The muscles of the left leg were also flabby and weak, but not to so great an extent as the right leg. The boy could support the weight of the body on the left leg. The knee-jerk was present on the left side, but on the right only a very slight contraction of the quadriceps extensor could be obtained.

The plantar response on the left side was flexor, but on the right a very definite extensor response was obtained (it seemed probable that the extensor response was dependent on the fact that the extensor muscles were comparatively well preserved, whereas the flexors were greatly affected).

Sensation over the trunk and limbs was perfect.

Electrical Reaction.—No reaction to faradism was obtained in the left deltoid, a very feeble contraction in the left biceps; the left supinator longus acted fairly. The muscles of the right arm reacted well.

Clinically the case appeared exactly like an extensive poliomyelitis, affecting both legs and the left arm, and had it not been for the history it would have been considered as a severe result of such a condition.

From November, 1901, until 1908, when the boy contracted diphtheria, he was constantly under my care.

He gradually learnt to walk, at first without any instrumental support, and after 1905, with the aid of an instrument, he was able to get about fairly well. His general health improved, but he always remained a thin and poorly nourished child. The shoulder-muscles of the left arm never regained any power.

In January, 1908, when eight years old, he contracted diphtheria, from which he died. With some difficulty permission was obtained to examine the brain and spinal cord, and a post-mortem was performed

in the Western Fever Hospital, thirty-six hours after death. The weather was cold, and the body was in good preservation. The membranes of the brain and spinal cord appeared normal on naked-eye examination. After hardening, the cord was carefully examined. All the dorsal roots appeared normal and of good size. On examining the ventral roots, it was obvious that those coming from the fifth cervical segment on the left side were smaller and greyer than those on the right side. The difference between the other cervical roots on the left side as compared to the right was not obvious. In the lumbar and sacral region again, although the roots appeared somewhat smaller than normal, yet no marked difference could be made out between the two sides.

Microscopical Examination.

The cord, after being hardened, was cut and stained by Van Gieson and Weigert-Pal methods. Sections were taken at various levels in the cervical, thoracic, lumbar, and sacral region of the cord.

Four typical sections will be described: (1) At the level of the fifth cervical segment; (2) at the level of the twelfth thoracic; (3) at the level of the third lumbar; and (4) at the level of the second sacral.

Van Gieson's Method.

(1) At the level of the fifth cervical segment the most striking change which is manifest is the very marked diminution in the number of cells in the region of the left ventral horn. The lateral portion of the ventral horn is that which is most affected—a small group of normal cells is seen in the ventral mesial group. On the right side the cells of the ventral horn are more numerous, but even here, as compared to a normal cord, it would be said that the cells were less numerous and smaller than normal.

No recent inflammatory change can be detected, nor is there any great increase of connective tissue, or remains of inflammatory products in the region of the horns.

(2) At the level of the twelfth thoracic segment there is a great diminution in the number of cells in the ventral horn on both sides, only one or two normal cells can be seen. The cells of Clarke's column are well developed on the one side, but are almost absent on the other.

The ventral roots as they pass through the white matter are most

poorly developed, and form but a small bundle after they leave the cord, and are in this respect in striking contrast to the dorsal roots.

(3) At the level of the third lumbar segment there is a great diminution in the number of cells in the ventral horn on both sides; a few scattered cells are present. The ventral roots are most poorly developed.

(4) At the level of the second sacral segment there are one or two well-developed groups of cells, but the relative number of cells is greatly diminished.

Weigert-Pal Method.

At the level of the fifth cervical segment (fig. 1) the left side of the cord is obviously smaller than the right. The whole of the antero-lateral tracts, with the exception of the dorsal and ventral cerebellar tracts, are

Right.

Left.

FIG. 1.

Section from the spinal cord at the level of the fifth cervical segment (stained by the Weigert-Pal method) showing diminution in size of the left side of the spinal cord, paleness of the fibres in the antero-lateral tracts, and a diminution in the number of the medullated fibres of the grey matter.

paler than normal. The grey matter on the left side is somewhat smaller than on the right, but the diminution of the medullated fibres in the grey matter on the left side is the most striking feature.

At the level of the first lumbar segment (fig. 2) the left side of the cord appears to be smaller than the right, and the grey matter of the ventral horn on that side is also smaller than that on the right side. The same paleness of the antero-lateral tracts is present as in the cervical segment; it is, however, more marked than in the cervical

region. The absence of medullated fibres in the ventral horns is also a striking feature.

At the level of the third lumbar segment (fig. 3) there is in both ventral horns a patch in which almost all medullated fibres appear to

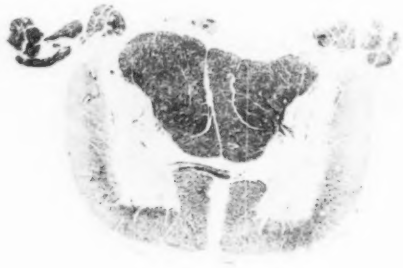

FIG. 2.

Section of the spinal cord at the level of the first lumbar segment (stained by the Weigert-Pal method) showing diminution in size of the ventral horn on the left side, and also a great diminution of the medullated fibres both in the grey and white matter of the cord.

FIG. 3.

Section of the spinal cord at the level of the third lumbar segment. The ventral horn of the left side is seen to be smaller than the right, but the most striking feature is the absence of medullated fibres in an area on the outer side of the right ventral horn, and also of a similar area in the left ventral horn.

be absent. The medullated fibres in the other portions of the grey matter of the anterior horn are diminished in number, being on the whole better preserved on the left side than on the right.

At the level of the second sacral segment (fig. 4) the diminution in the size of the cord on the left side is very obvious; on the other hand, there is a patch in the grey matter on the right side, in which nearly all the medullated fibres are absent.

The paleness of the antero-lateral tracts, as compared to the posterior columns, is very marked.

Shortly, it may be said that the most striking features are: (1) The diminution in size, not only of the cord, but also of the grey matter in the regions affected. (2) The presence of areas in the ventral horns in which there is an almost complete absence of medullated fibres. (3) The

FIG. 4.

Section of spinal cord at level of second sacral segment. The left side of the cord is seen to be smaller than the right, but in the grey matter of the right ventral horn there is seen to be an elongated patch, in which there is an almost complete disappearance of medullated fibres.

absence of large cells in the ventral horns of the regions of the spinal cord most affected. (4) The diminution in the size of certain ventral roots. (5) The paleness of the antero-lateral tracts.

The condition is exactly similar to that found in late cases of poliomyelitis [1].

CRITICISM.

I am fully aware that the above case is open to criticism, and the points that could be urged against the acceptance of this case as one of intra-uterine poliomyelitis are: (1) That the acute onset occurred

after birth, and escaped the notice of the mother. (2) That the condition is due to hæmorrhage into the grey matter of the spinal cord at the time of birth, resulting either from the rapid labour or the fall at birth. (3) That the condition is due to a developmental defect. (4) That the condition is due to an extensive and severe injury to the peripheral nerves, with consecutive atrophy in the cells of the ventral horn.

It will be well to answer these objections *seriatim*.

(1) It is well known that attacks of poliomyelitis not infrequently pass unobserved in infants. That, however, an attack of poliomyelitis, so severe as partially to paralyse both legs and give rise to a complete paralysis of the shoulder muscles, should occur without giving rise to any constitutional symptom is, I think, most improbable; and, further, we have the direct evidence of the mother that the left arm was paralysed at birth. It seems to me impossible to accept this interpretation.

(2) It is known that the delivery of the child was very rapid, and the child had a fall from the bed at the time of birth. It has been shown by Spencer [5] that hæmorrhage into the spinal cord not infrequently occurs in new-born children. The suggestion, therefore, that the condition might be due to hæmorrhage is one that requires to be carefully considered.

The hæmorrhage, to have caused such widely distributed paralysis, must have been an extensive one, involving both cervical, lumbar, and sacral regions of the cord. Pathologically, there is no evidence that such a hæmorrhage has occurred. Again, when hæmorrhage occurs into the spinal cord it commonly travels along the cord in the region of the root of the dorsal horns, and often leaves a cavity in this region. There is no evidence of such in the present case, and it seems to me most improbable that the spinal condition can be attributed to hæmorrhage taking place within the grey matter of the cord.

(3) That the condition might be due to arrested development in the spinal cord, is I think, a view that could hardly be held. The good development of the major portion of the nervous system, and the scattered nature of the change, quite apart from the character of the changes, make it inconceivable that arrested development can have played a part in the condition.

(4) That the condition was due to an extensive and severe injury to the nerves in some part of their peripheral course, with consecutive atrophy of the cells in the ventral horn.

It is well known that, as the result of damage to peripheral nerves, or amputation of a limb, the cells of the ventral horns undergo certain

changes, and may eventually atrophy completely. The condition is one of simple atrophy, and is not attended by changes seen in the white matter of the cord after extensive damage to the grey matter, such as have been shown to be present in this case.

From the clinical point of view, it is again difficult to accept such an interpretation, for the condition of the paralysed arm did not resemble that seen after a birth injury to the roots of the brachial plexus, and it also necessitates the assumption that the peripheral nerves of both legs were injured at birth—a condition which rarely occurs apart from severe and prolonged traction.

The absence of any affection of sensation might be added, although much stress could not be placed on this point, for in infants in whom the roots have been damaged it is most difficult to prove that there is any defect to painful stimuli. In the present case, however, had the extensive paralysis been due to a lesion of the peripheral nerves, it is almost impossible to believe that no sensory and no trophic loss would have resulted.

Although I am aware that the chain of evidence in this case is not complete, yet I think it may with good reason be accepted as one of poliomyelitis occurring during intra-uterine life.

Clinical and Pathological Examination of Case 2.

The second case is that of a female child, aged 2, who was admitted to the Children's Hospital under the care of Mr. F. J. Stewart with a history of hip trouble, which was said to have been congenital. On inquiry, however, it was found that the mother had not had charge of the child for a considerable time, and that the child had been in the infirmary.

On examination, the right leg was flexed, abducted and rotated out, and the head of the femur was so prominent that the condition was thought to be an anterior dislocation.

I saw the child, and, from the extremely flaccid condition of the muscles about the hip-joint and the very marked loss of power, came to the conclusion that the condition was probably one of late poliomyelitis.

The child was very ill at the time with broncho-pneumonia, following measles, and died a few days later, so that a complete and accurate examination of the muscular condition was never made.

The *post-mortem* was made and the spinal cord hardened. On

examination of the spinal roots in the lumbar and sacral regions, the dorsal roots appeared of normal size and equal on the two sides.

The ventral roots, however, showed a very marked difference between the two sides, this difference being most marked in the third lumbar root.

On section through the spinal cord, it was noticeable that the right side of the cord was considerably smaller than the left. The ventral horn on the right was much smaller than the left, and the nerve-cells in this region were very few in number. There was an area in the right horn in which the medullated fibres were very much diminished, and this is seen in the photograph as a pale, unstained area (fig. 5).

FIG. 5.

Section of cord at level of second lumbar segment (stained by the Weigert-Pal method). The right side of the cord is seen to be considerably smaller than the left, and the grey matter on that side is smaller and shows an area in which there is almost a complete absence of medullated fibres.

There is no doubt as to the nature of the case, but it may well be questioned whether the history of the case can be relied upon.

CONCLUSIONS.

(1) The cases recorded are clinically typical cases of the late results of acute poliomyelitis.

(2) The pathological condition found is that which is commonly found in late cases of poliomyelitis.

(3) In the first case the clinical history is so definite, and the child had been so long under observation, that there is but little reason for not accepting the history as correct and regarding the case as one of intra-uterine poliomyelitis.

In the second case it is fully realized that the clinical evidence is defective, and it is possible that the onset of the acute attack of poliomyelitis occurred after birth.

Finally, although the evidence brought forward is strongly in favour of the assumption that poliomyelitis does occur during intra-uterine life, yet it is fully realized that the chain of evidence is in some respects incomplete.

Having regard to the recent work of Flexner and Lewis [2], Landsteiner and Levaditi [4], and others, as to the infective nature of poliomyelitis, some test other than a pathological one may in future be applicable to these cases, and it will be possible to say, from a clinical examination of the blood, whether the child has or has not had poliomyelitis.

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Syphilis of the Nervous System.

Syphilis und Nervensystem. Von Professor Nonne. Berlin: Karger, 1909.

Syphilis of the Nervous System, by F. W. Mott, F.R.S., being vol. 4 of *A System of Syphilis.* Oxford Medical Publications, 1910.

Putting aside for the moment the parasyphilitic diseases, tabes dorsalis, and general paralysis, it is now generally recognized that the older view, enunciated by Fournier in his first edition, that syphilitic nervous disease seldom occurs in the first or second year after infection, is erroneous. Since the publication of Rumpf's [20] and Naunyn's [15] statistics, we know that syphilitic nervous disease is especially frequent within the first year, and, indeed, not rarely within the first month after infection. Naunyn, from the analysis of 335 cases, came to the conclusion that syphilitic lesions of the nervous system were most frequent in the first year after infection, and that 48 per cent. of all such cases occur in the first three years, and that their frequency gradually declines after that time. Gilles de la Tourette [6] has described an unusual and widespread case of severe syphilitic disease of the cerebral and spinal membranes, commencing two months after infection; and Head [8] refers to a case of a man who suffered from continuous headache from the first development of the chancre, the first definite signs of cerebrospinal syphilis developing after three months. The present writer [7] has seen an acute syphilitic paraplegia develop in a man three months after infection, while undergoing a course of mercurial treatment. In one of Nonne's cases severe basal meningitis, with cranial nerve paralysis and acute mania, developed four months after the infection during the course of the secondary rash. After the tenth year cerebral syphilis is exceptional, though there is no limit to its possible appearance; thus, Nonne saw a case with gummatous cerebral syphilis thirty years after infection, and Bruns [2] describes a case in which a large cerebral gumma grew forty years after the primary disease had been acquired. In Sigmund Kohn's [10] case the interval was also forty years.

Nonne's experience agrees with the statement that has been made that syphilis acquired in later life is more liable to strike the nervous system, and he finds that many of his patients who acquired syphilis between fifty and sixty became tabetic after some years. Syphilis in the aged generally runs a more severe course. Of late the question has been much discussed whether there is a special variety of syphilitic poison which is more liable to strike the nervous system, an affinity which may be compared with that of lead for the motor nerves and of ergot for the posterior columns. Numbers of instances of conjugal tabes and general paralysis of the insane in husband and wife have been recorded, which is suggestive evidence on this point. Mendel [13] described a case of a man who infected his wife with syphilis. The man died with general paralysis, and the woman married again and infected her second husband, both of them later developing tabes. Régis [18] published a case of a man who infected his wife and also her sister, all three of them subsequently developing general paralysis. More striking are those instances of a family type, in which tabes, general paralysis, and other syphilitic nerve diseases affect one or both parents, and one or more of their children. Thus in Remak's [19] case the mother developed cerebral syphilis, and her child juvenile tabes. In Nolan's [16] case the father had cerebral syphilis, and the child developed general paralysis. Such cases have been accounted for by the theory that the same heredity and similar surroundings are responsible for the selective action of the syphilitic poison on the nervous system, rather than that there is a special syphilitic neuro-toxin. Nonne gives reasons for disbelieving that the *milieu* is specially concerned in the development of familial syphilitic nervous disease, and he is of opinion that his own experience and also the literature prove that heredity and personal disposition also play no important part in its production. Some remarkable instances have been recorded in which several individuals infected from the same source at the same time have all later developed para-syphilitic nervous disease. Nonne narrates the case of three friends who were all infected in one night by the same woman; one became tabetic, and the other two developed general paralysis. Brosius [1] mentions seven glass-blowers who all developed chancre of the lip, being infected from the blowpipe. Five of these he was able to trace ten years later, and two were tabetic and two had general paralysis. Erb in 1904 related the case of five men all infected from the same source, and all became either tabetic or paretic. Lavallé also gives particulars of five men infected with syphilis at intervals from the same woman; three

of them died later of general paralysis, one of syphilitic meningitis, and the other of syphilitic dementia. Another instance recorded is of a man who acquired syphilis from his first wife, and he infected his second wife. Both the women died of general paralysis, but the man escaped. Hübner and others dispute the view of a special syphilitic neuro-toxin, but such facts as those related are strikingly suggestive, though not sufficient perhaps in themselves to establish the theory.

Two points of considerable importance which have been actively discussed are whether cerebrospinal syphilis, tabes, and general paralysis are less likely, or more likely, to follow slight or severe syphilitic infections, and whether the degree of thoroughness with which the syphilis was treated by mercury has any bearing on the after-development of these diseases. Rumpf [20] and others have pointed out that vascular syphilitic disease of the nervous system is due to an insufficient course of treatment for the primary infection, and Erb long ago declared that tabes occurred after slight infections in which no later symptoms arose, and in persons insufficiently treated. In 1903 Marie and Babinski confirmed this view. Neisser showed that of 445 cases of tabes, 57 per cent. had had no treatment for syphilis. On the other hand, Collins, in an analysis of his ninety-six cases, shows that energetic antisyphilitic treatment soon after infection does not prevent parasyphilitic disease of the nervous system developing later. Orlowski [17] came to the same conclusion, as, of seventy-two cases, in sixty-seven antisyphilitic treatment had been carried out, in twenty-three of them very thoroughly. Leyden and Herxheimer, and also Mauriac, go so far as to say that, as regards the development of later nervous symptoms, it is of no account whether the initial syphilis has been treated in the first or second stages thoroughly, or even not at all. Schuster [21] describes thirty-five cases of general paralysis—previously syphilitic—of whom twenty-one had been through one "cure," five had had two "cures," and six had been through from three to nine "cures." He also describes seventy-six patients with cerebrospinal syphilis who acknowledged antecedent syphilis, and twenty-four more who had been through from three to nine "cures" each. He finds no difference in the symptoms of those treated and those who never had antisyphilitic treatment, and the average period of incubation in the treated and in the untreated is much the same. He, too, comes to the conclusion that the idea is false or unproved that mercurial treatment stops or delays the onset of syphilitic or parasyphilitic disease of the nervous system. Nonne also recognized five years ago that

in many cases of syphilitic or parasyphilitic nervous disease the mercurial treatment had been most thoroughly carried out; and in two cases, when the nervous complications occurred within the first two years, the treatment had been carried on uninterruptedly from the beginning. As a contrast to these he quotes the case of an officer who became infected with syphilis, but had no treatment for the disease; four months later he developed severe brain-syphilis, which proved fatal. Some good observers are of opinion that brain-syphilis is especially apt to follow the slighter syphilitic infections, but this view does not accord with Nonne's experience. Mott agrees with Nonne, Fournier, and others, that there can be no question of the beneficial effect of early treatment of the primary disease, and that nervous affections are more likely to occur when mercurial treatment has been either insufficient or not practised at all. The point may therefore be still considered unsettled whether early treatment is beneficial or is of no influence in averting subsequent nervous syphilis, but, on the whole, the balance of evidence probably lies in favour of those who advocate the earliest and most systematic course of cure for the primary disease. The conflicting views may perhaps be accounted for by the fact that, as Mott observes, once the *Spirochæte pallida* has gained access to the subarachnoid space and has infected the central nervous system, it is most difficult, if not impossible, to dislodge. In many cases this infection of the nervous system takes place quite early, within the first weeks after the acquirement of the chancre, and thus cerebrospinal syphilis, or later metasyphilitic disease of the nervous system, may follow in spite of the most prolonged and thorough course of mercurial cures. Yet, in those cases in which this infection of the central nervous system with the spirochætes has not as yet taken place, energetic mercurial treatment may be fortunate enough to produce a complete cure and prevent the subsequent development of syphilitic nervous disease. A somewhat similar argument has been put forward in the case of diphtheria, that since the introduction of antitoxin the number of cases of diphtheritic paralysis is greater, and therefore due directly to the use of the antitoxin. The explanation of this seeming paradox lies in the fact that many of the severe cases which formerly would have died are now saved by the use of the antitoxin, and later development of neuritis is due to the severity of the diphtheritic infection and not to the use of the antitoxin.

With regard to the development of the parasyphilitic diseases, tabes and general paralysis, the idea is held by some that not only are

mercurial inunctions and other forms of antisyphilitic treatment useless for the cure of these diseases, but that, being neuronal degenerations, the mercury does actual harm by lowering the degree of vital resistance of the tissues, hence hastening the process of neuronal decay. In favour of this view are the observations, familiar to the practice of most physicians, of the startlingly rapid increase in the delusions and mental excitement of an early case of general paralysis, perhaps classed as doubtful, during the course of an energetic administration of mercurial inunction; or, again, a pronounced intensification of the lightning pains and other symptoms of tabes in a patient with the early signs of this disease when similarly treated. On the other hand, many excellent clinicians are firmly convinced that they have seen many cases of undoubted tabes, if not of general paralysis, who have remained apparently permanently improved after the administration of long courses of mercury and iodide of potassium, which such patients sometimes appear to be able to absorb for longer periods without showing symptoms of mercurialism than the average patient. It is difficult to convince such observers that they have been mistaken in their diagnosis, and that these cases which have been benefited by antisyphilitic treatment were not really cases of tabes or general paralysis, but syphilitic pseudo-tabes and pseudo-paresis.

One view [Mott] of the etiology of the parasyphilitic diseases, tabes and general paralysis, which must be mentioned is based on Ehrlich's theory of the artificial production of immunity against disease. It is supposed that there is an inherent aptitude for the cells of the body of certain individuals to adapt themselves readily for defence against the action of the syphilitic virus in a race that has been widely syphilized for generations; consequently a larger number will have a mild form of the disease. The nerve cells are perpetual elements incapable of regeneration, highly differentiated and complex in structure and function; their centre of nutrition is the nucleus, and when decay sets in the retrogressive process attacks first the fine twigs and branches and rootlets of the tree, the dendrites and dendrons; in fact the process is an inversion of its growth and development. We know the prolonged duration of infectivity of the syphilitic virus as compared with other contagious diseases, also that one attack of syphilis as a rule confers immunity during the rest of the individual's life. Hence, the nerve-elements being perpetual, and having acquired a habit of throwing off side-chain molecules, will continue to do so during life, and will contribute largely to the immunity produced. When there is no longer

metabolic equilibrium and decay of the neuron sets in, these antibodies are thrown off in increasing numbers, as shown by the presence of serum albumin in the cerebrospinal fluid, and the positive reaction of this fluid to the Wassermann test for syphilis, although in cerebrospinal syphilis this fluid gives a negative reaction when the blood serum is positive to the test. That the antibodies are thrown off in increasing numbers seems probable from the fact that in general paralysis and tabes the quantities found in the cerebrospinal fluid increase with the progress of the decay; for Marie and Levaditi [12] have shown that there is a parallelism between the rapidity of progress of general paralysis and the degree of intensity of the Wassermann reaction. No doubt, therefore, there is a connexion between the breaking down of nervous substances (destructive metabolism) and the amount of this complex colloidal substance, with which probably the reaction is associated and upon which it depends.

The spinal cord is much less frequently affected by syphilitic disease than is the brain, in the proportion of one spinal case to eight or ten cerebral. Spinal syphilis is much less serious, on the whole, than brain syphilis, though in the majority of fatal cases of syphilis of the nervous system both brain and spinal cord have been found affected. It is, in fact, a constant anatomical finding that the syphilitic lesions of meninges, vessels, and cord are invariably much more widespread than the symptoms would lead one to suppose; and though the symptoms may be entirely spinal, and apparently focal, widespread lesions are likely to be found, involving the brain in addition to the spinal cord. Thus Siemerling showed that extensive syphilitic changes in the brain can remain latent during life, and also that spinal changes may be latent in apparently pure cerebral syphilis. In Weygandt's case, clinically one of pure cerebral syphilis, widespread vascular changes in the cord down to the lumbar region were found post-mortem. In Nonne's case of apparently pure severe transverse lumbar myelitis he found post-mortem, in addition to a gummatous meningo-myelitis, an extensive gummatous infiltration at the base of the pons, and in the interpeduncular space. Cerebrospinal syphilis, like primary syphilis, is much more frequent in men than in women. The influence of a neuropathic disposition in the etiology of spinal syphilis is not known, but spinal trauma and functional overstrain have been definitely shown to be exciting factors in its development. Thus, a sailor, ten years syphilitic, received severe blows on his back during a storm. Six months later the first symptoms of meningo-myelitis appeared, which

did not react to treatment with mercury and iodide. After five years' illness he died, and post-mortem widespread meningo-myelitis, with severe vascular changes, was found. The present writer has seen a similar clinical result follow a slight spinal injury: a man, aged 26, jarred his back by a fall from a sofa; immediately afterwards he noticed a numb feeling in the lower part of his back, and this numbness, varied by occasional pains, has troubled him ever since. Six months later he developed pains round the lower ribs and in the legs, and two and three-quarter years later he developed internal ophthalmoplegia, first in one eye and later in the other. A year later the pains in the back and legs increased, and weakness of the legs appeared, with all the symptoms of an organic spastic paraplegia, which cleared up almost completely after thirteen weeks of mercurial treatment. Though he denied all venereal disease, the Wassermann test was positive. It is easy, however, to overstate the effect of trauma in producing cerebrospinal syphilis, and Nonne, in a large experience, saw only two cases in which cerebral syphilis definitely followed, in one case two weeks and in the other three months, after a severe blow on the head. A case of Fournier's illustrates the effect of overstrain of the spinal functions. A man took a long and severe bicycle ride, and almost immediately after developed pains in the back, bladder-weakness, progressive paraplegia, and died of a characteristic syphilitic myelitis. The question whether cerebrospinal syphilis and the meta-syphilitic diseases, tabes and general paralysis, may be actually developed as the result of injury to spine or head in a syphilitic subject is a point of considerable medico-legal importance, and the question as to whether the symptoms would not have developed in any case is one almost impossible to decide definitely. Mott points out the well-known fact that traumatic neurasthenia is frequently seen as the result of injuries to head or spine, and he argues that in a syphilitic subject such a nervous system is a *locus minoris resistentiæ*, and that general paralysis may develop as the sequel of such a condition when it would never have appeared without the antecedent injury.

Nonne classes syphilitic lesions of the nervous system under three headings: (1) Gummatous new growths; (2) Chronic hyperplastic inflammations; (3) Vascular disease. Gummata of the dura or of the spinal cord alone are rare, though more frequent in the brain. By far the most frequent lesion is a diffuse meningo-myelitis, in which the gummatous hyperplastic inflammation invades the leptomeninges, spinal cord and roots, with widespread vascular disease, affecting both arteries and veins alike with endo- and peri-arteritis, and endo- and peri-phlebitis.

As a result of thrombosis or occlusion of vessels, patches of softening with hæmorrhage may occur in the grey as well as the white matter. The picture of acute myelitis may thus be produced, which we should not be justified in ascribing to syphilis, unless there were a history or signs of syphilitic disease, and a condition of the vessels as has been described. When the grey matter is affected an acute poliomyelitis may occur, followed by atrophic muscular paralysis. Spiller describes such a case affecting all four limbs, due to syphilitic thrombosis of the anterior median spinal artery. Subacute poliomyelitis may also occur, affecting generally the upper extremities. Mott explains the frequency of syphilitic transverse myelitis in the mid-dorsal region by the particularly poor blood supply of this region of the cord, and he also suggests that the chronic venous congestion and peri-arterial inflammation which occurs in an acute gummatous meningitis would leave behind a slow sclerosing fibrosis most intense, and most likely to result in a chronic fibrous infiltration along the pial septa enclosing the nutrient vessels of the cord substance. He would thus explain the pathology of Erb's syphilitic spinal paralysis, this theory avoiding the necessity of assuming a primary degenerative process affecting the pyramidal system below the dorsal region.

Although there are not wanting authorities in the French school, Nageotte, Leredde, &c., who assert that tabes and general paralysis are secondary nerve degenerations following a chronic syphilitic radicular neuritis and meningitis, yet it is generally assumed that these degenerations are primary and parasyphilitic, not dependent upon any true syphilitic process, and therefore not curable by antisyphilitic remedies. Mott and others declare that so-called cures of tabes and general paralysis by mercurial inunction were not really cases of tabes and general paralysis, but instances of pseudo-tabes and pseudo-paresis, due to a chronic diffuse meningeal and radicular inflammation of syphilitic origin. Many cases of so-called primary tract degenerations of the pyramidal tracts and postero-lateral columns have been recorded, but many of them are open to the explanation given by Mott of antecedent damage from meningeal inflammation to the nutrient vessels of the cord in the mid-dorsal region. Others may be due, as Gordon Holmes showed in a recent case, to a primary focal softening at a distance, such as symmetrical pyramidal degeneration due to a patch of softening in the pyramidal decussation in the medulla. Optic atrophy, apparently primary, may be similarly traced to an unsuspected focus of gummatous infiltration of the chiasma. Nerve-cell degenerations appear to be sometimes primary, notably the

well-known sclerotic degeneration of the third, fourth, and sixth cranial nerve nuclei, known as nuclear palsy.

The examination of the cerebrospinal fluid gives very valuable help in the differential diagnosis of general paralysis from neurasthenia and alcoholism. The presence of a mononuclear lymphocytosis will at once exclude the latter. Lymphocytosis alone is not certain proof of a meningeal reaction, and has been met in herpes zoster, subacute combined sclerosis, &c. In syphilitic meningo-myelitis the cell count in the cerebrospinal fluid will be especially high, much higher than in any case of tabes or general paralysis, though in the latter the lymphocytosis will not diminish under mercurial treatment, while in syphilitic spinal disease the leucocytosis will gradually disappear under treatment. The proteid content of the fluid is notably increased in tabes, and especially general paralysis. In normal cerebrospinal fluid there is a trace of globulin present, but albumin is absent. In parasyphilis the globulin is much increased, and it may be precipitated by saturation with magnesium sulphate, and after filtration further saturation with ammonium sulphate will demonstrate the presence of serum albumin. In addition to this chemical test and the examination of the cell exudate, the examination of the fluid for the Wassermann serum reaction for syphilis will be of great service. Mott declares that in parasyphilis, especially general paralysis, the cerebrospinal fluid will give a positive reaction to the Wassermann test, as well as the blood serum; that is to say, in over 90 per cent. of cases of general paralysis the reaction in the cerebrospinal fluid is positive, while in other syphilitic affections of the nervous system, such as meningo-myelitis, syphilitic arteritis, &c., the cerebrospinal fluid will give a negative reaction to this test, although the reaction in the blood may be positive. Mott quotes a very instructive case in which this point alone decided the diagnosis in a case of general paralysis, in which the clinical symptoms were mainly misleading. According to this teaching, the Wassermann reaction used in association with a lymphocytic count will become all-important in the diagnosis of syphilis and parasyphilis of the nervous system. Thus: (1) A positive reaction in the blood with a negative reaction in the cerebrospinal fluid and no lymphocytosis indicates that though the patient has had syphilis it has not affected his nervous system; (2) A positive reaction in the blood, a negative reaction in the cerebrospinal fluid, and definite lymphocytosis signify that he is suffering from active syphilis of the central nervous system: (3) A positive reaction in the blood with a positive reaction in the cerebrospinal fluid and a lymphocytosis points to a

parasyphilitic condition of the central nervous system. If these reactions are found to be trustworthy we shall have gained a most valuable means of diagnosis.

WILFRED HARRIS.

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Publications Recently Received.

[*Notes on a book under this heading do not preclude a subsequent review.*]

Epidemic Poliomyelitis. Report of the Collective Investigation Committee on the New York Epidemic of 1907. Pp. 119. New York: Journal of Nervous and Mental Disease Publishing Co., 1910.

During the summer and autumn of 1907, at least 2,500 cases of poliomyelitis occurred in New York and its vicinity. The Neurological Society formed a committee to investigate this epidemic, and this pamphlet contains the results it obtained. The incubation period was from four days to about a week: but in no case did the circumstances permit of its certain determination. No cause was discovered, and the disease attacked mainly young children. Pain was a common symptom, and meningeal affection was frequent, especially in the early stages. As usual, abortive forms occurred sufficiently often to confirm the statements of the Swedish observers. No single case of cerebral affection or infantile hemiplegia occurred during the epidemic. Flexner and Lewis give an account of the means by which they were able to transmit the disease from two human cords to two monkeys, and from them to a series of other monkeys by intracranial injection. They could find no organisms of any kind, and the virus passed through a filter and withstood glycerinization; it is therefore not bacterial in nature.

A System of Syphilis, in Six Volumes: Vol. IV., Syphilis of the Nervous System. By F. W. Mott, M.D., F.R.S. Pp. 502, with many plates and illustrations in the text. London: Frowde and Hodder and Stoughton, 1910.

This magnificent work is the first comprehensive statement in English of the relation between syphilis and diseases of the nervous system in the light of recent additions to our knowledge. Dr. Mott, in the first five chapters, deals with the general pathology of syphilis of the nervous system, the symptoms of

syphilis of the brain and of the spinal cord, and the parasyphilitic diseases. Then follows a valuable chapter on the cerebrospinal fluid, with a full discussion of the diagnostic value of the Wassermann reaction in syphilis and parasyphilis of the nervous system. More than seventy pages are devoted to the etiology of tabes dorsalis and dementia paralytica, and the symptoms of tabes are dealt with consecutively later in the volume. A chapter is devoted to the difficulties of diagnosis and treatment fully considered. Dr. Mott ranks himself definitely amongst those who believe that mercurial treatment is useless or even harmful in parasyphilis. The plates are admirable, but a few of the figures in the text will probably be improved in a second edition. For there is no doubt that this work will become the standard hand-book for English practitioners.

Die Trypanosomenkrankheiten und ihre Beziehungen zu den syphilogenen Nervenkrankheiten. Von Dr. Walther Spielmeyer. Mit 6 Tafeln. S. 106. Jena: Fischer, 1908.

The discovery of the *Spirochaete pallida* has added peculiar interest to all diseases due to invasion of the body by trypanosomes. This work gives the pathological appearances found in sleeping-sickness and in experimental trypanosomiasis. The author concludes that the sum of clinical and anatomical appearances points to a relationship between trypanosomiasis and its consequences and syphilis and parasyphilis. Dourine is normally contracted by the horse during connexion, all trypanosome diseases tend to affect the lymphatic glands, and all tend to produce system-degenerations in the nervous system. The coloured plates are excellent.

Das psychogalvanische Reflexphänomen. Von Dr. Otto Veraguth. Mit 44 Abbildungen. S. 187. Berlin: Karger, 1909.

Dr. Veraguth was the first to use galvanometric changes in the normal skin currents as a test for psycho-physical disturbances. This method was adopted by Jung for registering the disturbances discovered by psycho-analysis, and a paper on the subject appeared in *Brain*, 1907. The inventor of the method has now put together his experiences in a careful monograph dealing with the technique and results he has obtained. There seems to be no doubt that the galvanometer can give undoubted indications of affective disturbances which arise in the course of a psycho-analytical examination. The galvanometer curves run parallel in most cases with the reaction-time records, and evidently are affected by the same emotional factors. The book is written with a commendable absence of the exaggerated claims put forward by some of those who have worked with this method.

Ueber die medizinischen Folgezustände der Katastrophe von Courrières [10 März, 1906]. Von Dr. EDUARD STIERLIN. S. 188. Berlin: Karger, 1909.

The author investigated the condition of the miners saved from the pit after the disaster at Courrières. He watched them in some cases for two and half years, and compares the result of his observations with the conditions he found after the earthquake at Valparaiso and that in the South of Italy. The work is an interesting contribution to our knowledge of traumatic neuroses, on account of the full clinical histories, and careful examination of the sufferers. In some cases of pronounced carbonic-oxide poisoning, a dementia resulted closely resembling that produced by gross organic disease: some cases showed all the signs of a severe traumatic hysteria. Unfortunately, like so many German monographs, this book has no index.

Reports from the Pathological Laboratory of the Lunacy Department [*New South Wales Government*]. Vol. II. Part I. Sydney: The Government of the State of New South Wales, 1910.

This volume contains a paper by Dr. Flashman and Dr. Latham on the pathology of general paralysis, with special reference to the action of diphtheroid organisms, in which they came to the conclusion that "diphtheroid organisms administered in a suitable way over a long period can produce marked cerebral changes, the chief of which are overgrowth of neuroglia, periarteritis, chronic thickening of the pia-arachnoid and destruction of neurones." A paper by Dr. Flashman and Dr. Butler deals with the Wassermann reaction in syphilis and general paralysis; their results confirm those of Mott and other workers. There are also two small papers by Dr. Flashman on degenerations following resection of the optic lobe and portions of the cortex in Dasyurus Viverrinus.

Gehirn und Schädel. Eine topographisch-anatomische Studie in photographischer Darstellung. Von Dr. Fr. HERMANN. Mit 69 zum Teil mehrfarbigen Lichtdrucktafeln. Jena: Fischer, 1908.

This article contains the photographic reproductions of the contents of the cranial cavity, from the moment the skull cap is removed to the last of a series of sections. The first twenty-three plates show sections taken at a slightly inclined horizontal level. Then follow a set of vertical sections from before backwards and from behind forwards, so as to include the relations of the cerebellum. These are followed by a series of sagittal views of various parts of the brain. To every plate is attached an explanatory figure, generally in the form of a transparent cover, upon which the various structures are

named that are visible on the photograph. Medical libraries should possess this work, which will be useful to those unfamiliar with the topographical relations of the various regions of the brain to the skull.

Physiology of the Special Senses. By MAJOR GREENWOOD, Junr. Pp. 239. London: Arnold, 1910.

This book is intended as a companion to the "Text-book of Experimental Psychology" by Dr. Myers, and will be useful to those who are working for one of the higher examinations. So much of our knowledge of the physiology of the special senses is recently acquired that it is peculiarly difficult to present the various subjects clearly, and at the same time to refrain from accepting some highly controversial standpoint. But, as far as the space at his disposal permits, Dr. Greenwood has given an excellent critical account of recent work. The senses are considered in order, beginning with those of the skin and subcutaneous structures. More than half the book is occupied with various problems in vision, and a chapter is devoted to each of the two main theories of colour vision. The advice to the student with regard to further study at the end of each chapter is uniformly excellent.

Handbuch der Neurologie. Herausgegeben von M. LEWANDOWSKY. Erster Band—Allgemeine Neurologie, I and II Theil. S. 1606, with 322 figures and 12 plates. Berlin: Springer, 1910.

This valuable work forms the first volume of a System of Neurology. Here the various departments of neurological knowledge are treated at sufficient length to make them useful to the serious worker in the subject. It contains over 1,600 pages, and deals with the histology, the anatomy, and the experimental physiology and pathology of the nervous system. The last part of the book deals fully with the treatment of nervous diseases. The different chapters maintain a remarkably high level, and, although closely packed with information, are unusually readable. If the remaining volumes are as good as the first, this hand-book will be indispensable for every neurologist.

A Text-book of Nervous Diseases. By WILLIAM ALDREN TURNER, M.D., and THOMAS GRAINGER STEWART, M.B. Pp. 607. London: Churchill, 1910.

This text-book is well suited to the needs of the practitioner and senior student. It is clearly and succinctly written, it is thoroughly up to date, and the illustrations are excellent.

Die Indikationen zu chirurgischen Eingriffen bei inneren Erkrankungen. Von Prof. Dr. HERMANN SCHLESINGER. Mit einem Anhange von Prof. Dr. JULIUS SCHNITZLER. S. 614. Jena: Fischer, 1910.

The portion of this volume of interest to neurologists comprises just over 100 pages, devoted to surgical measures adopted in diseases of the nervous system. Owing to the limitations of the work, the differential diagnosis and indications for operation in cases of tumour and abscess of the brain are not given with sufficient fulness to be of much value. Epilepsy, primary and secondary to trauma or local brain disease, is treated in a few detached paragraphs. Laminectomy and operations on the peripheral nervous system are dealt with as if the author had no personal experience of such procedures and was ignorant of the measures usually adopted in this country.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.